

**DEPARTMENTS OF LABOR, HEALTH AND
HUMAN SERVICES, EDUCATION, AND RE-
LATED AGENCIES APPROPRIATIONS FOR
FISCAL YEAR 2007**

FRIDAY, MAY 19, 2006

U.S. SENATE,
SUBCOMMITTEE OF THE COMMITTEE ON APPROPRIATIONS,
Washington, DC.

The subcommittee met, at 8:31 a.m., in room SD-192, Dirksen
Senate Office Building, Hon. Arlen Specter (chairman) presiding.
Present: Senators Specter, Shelby, and Harkin.

DEPARTMENT OF HEALTH AND HUMAN SERVICES

NATIONAL INSTITUTES OF HEALTH

STATEMENT OF ELIAS A. ZERHOUNI, M.D., DIRECTOR

ACCOMPANIED BY:

**JOHN E. NIEDERHUBER, M.D., ACTING DIRECTOR, NATIONAL CAN-
CER INSTITUTE**

**FRANCIS S. COLLINS, M.D., DIRECTOR, NATIONAL HUMAN GENOME
RESEARCH INSTITUTE**

**ANTHONY S. FAUCI, M.D., DIRECTOR, NATIONAL INSTITUTE OF AL-
LERGY AND INFECTIOUS DISEASES**

**ELIZABETH G. NABEL, M.D., DIRECTOR, NATIONAL HEART, LUNG,
AND BLOOD INSTITUTE**

OPENING STATEMENT OF SENATOR ARLEN SPECTER

Senator SPECTER. Good morning, ladies and gentlemen. The Ap-
propriations Subcommittee on Labor, Health, Human Services,
Education, and Related Agencies will proceed with this hearing on
the National Institutes of Health, and the funding for these insti-
tutes. We have a rather unusual hearing this morning because we
have asked representatives of groups advocating research on the
major illnesses—heart, cancer, Alzheimer's, Parkinson's—some 20
in total, to underscore the difficulties facing medical research in
the United States today.

As it is well known, this subcommittee, Senator Harkin and I,
have taken the lead on NIH funding, which has grown from \$12
billion to \$29 billion over the past 10 years. Now we have seen the
increases which we had structured by, candidly, robbing Peter to
pay Paul. We have a very complex budget on this subcommittee
which has to fund not only health but education, labor, worker
safety, Head Start, the bulk of the social programs.

Those programs have been cut in the last 2 fiscal years, taking into account actual cuts and inflation, cut by some \$15.7 billion. The NIH, which I frequently say is the crown jewel of the Federal Government, if not the only jewel of the Federal Government, has been cut 10.4 percent in the last 2 years. We find that in fiscal year 2006 there was an actual cut of almost \$66 million.

The funding for fiscal year 2007 is level by the administration. That means with the inflationary increase there is a decrease in the actual dollars which are available. That is just unacceptable in a country with an \$11 trillion gross national product and a Federal budget of \$2.8 trillion.

The advances that have been made by medical science are really remarkable, but it takes funding to accomplish that. Something personal to me is the lack of adequate funding for the National Cancer Institute. In 1970 President Nixon declared war on cancer and if that war had been pursued with the same intensity as our other wars cancer would have been cured long ago.

My chief of staff, Carey Lackman, a beautiful young woman of 48, died of cancer, breast cancer, recently. My son's partner's wife, a beautiful young woman, died of breast cancer. One of my best friends, Judge Edward Becker, one of the most distinguished jurists in America, is suffering great anguish and great pain as we speak from prostate cancer. I had a bout with Hodgkin's last year myself and if you see me dabbing my eyes that is one of the remnants of chemotherapy. Had the Nixon war on cancer been pursued, I think I would not have gotten Hodgkin's and Carey Lackman would not have died, Paula Klein would not have died, Ed Becker would not be in the dire straits he is today.

It is just unconscionable that we are not doing more. That is tied to stem cell research. Again, Senator Harkin and I have taken the lead there with our legislation which would enable, authorize, take the bar away from the Federal Government supporting embryonic stem cell research. We had a meeting yesterday with Senator Frist, the Majority Leader. I believe we are going to have a vote very soon on our issue. It is doubtful that we have 67 to override a presidential veto and we are talking about organizing a march on The Mall. We would like to put 1 million people on The Mall in September, enough people on The Mall to be heard in the living quarters of the White House just a few blocks away, because the estimate of 110 million people being affected directly or indirectly by these ailments is enough to produce two-thirds to override a presidential veto if in fact the President carries out his statement that he will veto the bill.

Well, we have a very long hearing today. We moved the hearing from 9:30 to 9:00 and then we moved it from 9:00 to 8:30 because Senator Harkin has commitments in Iowa. I am a little more flexible. I only have to travel to Pennsylvania. But we have a hearing this afternoon in Philadelphia on campus safety. It is a very, very busy Congress and I think you have seen that from the activities on the confirmation of the Supreme Court justices and the immigration bill, the Patriot Act, and so many other things we are doing.

But I do not believe there is any subject as important as this one. You keep hearing "nothing more important." Well, we may be tied

for first place. I do not think that it is true that there is no subject more important than this one. I do not think there is any subject as important as this one. This is number one. Without health there is nothing.

Senator Harkin.

STATEMENT OF SENATOR TOM HARKIN

Senator HARKIN. Mr. Chairman, thank you very much for your very eloquent opening statement. I would ask that all my statement be made a part of the record. I will just comment on it here.

First, let me thank you, Mr. Chairman, for your courageous leadership in this area of always fighting for the funding we need for NIH. You led the way on building the funding over those years. I was happy to backstop you and support you in that. It was a very courageous effort that you led on that.

I thank you also for your courage in speaking out on the budget earlier this year and your continuing to speak out against the budget as it affects NIH.

Let me also thank you for your own personal courage in battling Hodgkin's lymphoma last year and the example that you set in coming to work every day and holding the hearings in the Judiciary Committee and the Supreme Court nominees and taking it to the floor even while you were undergoing some pretty severe chemotherapy. So it was a great example, I think, of personal courage and we thank you for that.

I would just remind everyone of what Senator Hatfield said. When Senator Hatfield left the Senate, he gave his final speech on the Senate floor. I will never forget. I was over there to listen to it. He said at the time, he said: It is not that the Russians are coming. He said: It is the viruses are coming, the viruses are coming. How prophetic, how prophetic.

We did not work hard to double the funding of NIH to then have it plateau off for another 20 years. The idea was to get it back up where it had been in the 70s, where we had some 40-some percent of our peer reviewed grants approved and funded. That had fallen down and now I think it is down to about—I do not have it in front of me. I think it is down to about 19 percent right now, the lowest ever, the lowest ever.

The problem—not only is it a problem this year in terms of the budget—yes, it is 19 percent right now. About one out of every five is accepted for funding. I think that is having a ripple effect on researchers, it is having an effect on young people who are thinking about research as a lifetime avocation.

But the problem is also looking ahead. As bad as this year's budget is, next year's could be worse. According to OMB projections, the administration will cut NIH by \$800 million in 2008 and make more cuts in 2009 and fiscal year 2010.

Something has got to be done about this. Again, Senator Specter, you have been tremendously courageous in speaking out and trying to get a better deal for us on the budget. But we need to hear from you at NIH, but we also need to hear from the groups that are coming later, to tell the human side and give the human face as to what is happening to so many people in our society.

PREPARED STATEMENT

I have a friend of mine who at this very moment is in the final stages of ALS disease. It is one of the worst things you can imagine. Yet we dither around and we cannot get stem cell research going in this country?

Well, again, Mr. Chairman, thank you. It has been an honor to work with you.

[The statement follows:]

PREPARED STATEMENT OF SENATOR TOM HARKIN

Thank you, Mr. Chairman. You've led the way on NIH funding, and it's been a real honor working with you on this issue.

Good morning, Dr. Zerhouni, and welcome. We're glad to have you back with us today.

We need a strong NIH now more than ever, for so many reasons. First, our security as a Nation depends on it. We often think about security only in military terms. But in today's world, we need to be just as worried about the threats we face from a bioterrorism attack or pandemic flu. NIH research is critically important for protecting us in both of those areas.

We also need NIH to help us through our health care crisis. Consider just one disease—Alzheimer's. It's been estimated that delaying the onset of Alzheimer's by just 5 years could save \$50 billion a year in medical costs. That would go a long way to solving our Medicare problems all by itself.

We need NIH now, because we're on the cusp of so many exciting breakthroughs. Researchers are learning how to match drugs to individual patients, based on their genetic code. They're learning more about stem cell research. They're making discoveries about the interplay between our genes and the environment.

What a shame, then, to get a budget like the one the President has sent us.

His budget would level-fund NIH, one year after the first cut to this agency since 1970. Eighteen of the 19 institutes would get less funding than they did last year. The number of research project grants would drop by about 640. And the success rate for grant applications would remain at a record low of just 19 percent.

We're at a point now where only 1 out of every 5 grant applications is accepted for funding. I'm sure there are a lot of young researchers out there who are wondering, "Why bother applying to NIH? Why bother going into research at all?"

Senator Specter and I didn't work so hard to double NIH funding just so we could watch the President cut it to the bone from then on out. But that seems to be the President's plan. As bad as this year's budget is, next year's will probably be even worse. According to OMB projections, the Administration will cut NIH by \$800 million in fiscal year 2008, and make more cuts in fiscal year 2009 and fiscal year 2010.

We're going to hear firsthand what the President's budget will mean for many diseases from our second group of speakers. I want to thank the representatives of the 20 advocacy groups that are with us today for taking the time to be here.

Mr. Chairman, I look forward to the testimony.

Senator SPECTER. Thank you very much, Senator Harkin. Thank you for your leadership on these issues and the partnership which I think has been very productive for our country.

Senator Shelby.

STATEMENT OF SENATOR RICHARD C. SHELBY

Senator SHELBY. Thank you, Mr. Chairman. Mr. Chairman, I ask that my written statement be made part of the record and I will be brief.

This is a very important hearing and I am here this morning to help you. I think the President, George W. Bush, is going to have to speak out on this issue, that is properly funding NIH medical research. We are falling behind and we cannot, because we have led the world. We continue to lead the world, although we are struggling as far as finances are concerned.

Mr. Chairman, you and Senator Harkin, who are the leaders of this committee, I can tell you I am going to do everything I can. We are challenged in the research everywhere in biomedical, but in autoimmune areas there is a lot of hope there. I am particularly interested in the lupus area. We are challenged there. I am going to do everything I can as a member of the Appropriations Committee to help fund, properly fund, medical research through NIH. You have made a difference and you will make a tremendous difference in the future.

PREPARED STATEMENT

But, as Senators Specter and Harkin both know, it is not going to be easy, but we cannot go backward. We cannot cede this to anybody else in the world. We are the leaders. We have got to stay there.

Thank you, Mr. Chairman.
[The statement follows:]

PREPARED STATEMENT OF SENATOR RICHARD C. SHELBY

Mr. Chairman, thank you for holding this important hearing today. I want to thank all of you for taking the time to be here today. It is vitally important for me to hear directly from you on what your agency's needs are, and the challenges you might face in the coming months. We as a Nation are facing a integral moment in funding critical research. Finding viable treatments and possible cures for many of our common afflictions is our most important goal, but I think early detection of disease is fundamentally important to containing costs in the long-term.

As we begin to move forward in the appropriations process it is of the utmost importance that we ensure adequate funding for these indispensable research institutions. Millions of Americans rely on the life saving work they perform and it is imperative that we as appropriators fully support them.

Federal funding for medical research is critical and while we have worked diligently to increase funding, more is left to do.

I am hopeful that this hearing today will provide a forum to discuss the issues that must be addressed by researchers.

Thank you for your time and I look forward to your testimony.

Senator SPECTER. Thank you very much, Senator Shelby.

We now welcome Dr. Elias Zerhouni, the Director of the National Institutes of Health. He had an illustrious career before coming to be the 15 Director of NIH. He had been executive vice dean at Johns Hopkins University School of Medicine, chair of the Department of Radiology and Radiological Science. He received his medical degree from the University of Algiers School of Medicine and completed his residency in diagnostic radiology at Johns Hopkins.

Thank you for your leadership in this very vital area, Dr. Zerhouni, and we look forward to your testimony.

SUMMARY STATEMENT OF DR. ELIAS A. ZERHOUNI

Dr. ZERHOUNI. Thank you, Mr. Chairman. Thank you, Senator Harkin, Senator Shelby. I submitted a written testimony. What I would like to do really is just summarize the salient points of the testimony, to allow as much time as possible for questions.

Senator SPECTER. Thank you, Dr. Zerhouni.

Dr. ZERHOUNI. What I would like to do is really direct your attention to the screens.

RETURN ON INVESTMENT ON NIH FUNDING

What I would like to address are the fundamental questions that I think all of us would like to have an answer to, to be able to set policy for the future. First and foremost, what is the return on the American people's investment at the National Institutes of Health? Second, what has this NIH budget doubling delivered for the American people? Third, what is our future strategy? Where is NIH heading? When you talk about medical research it is important to understand that it is not a 100-meter dash, it is a marathon, and we have to sustain the effort over time.

First, let me just remind everyone that biomedical research has delivered enormous returns to the American people. I am just going to give two examples here. Many more are in the testimony. In coronary heart disease, if you look at the progress over the past 30 years, there has been a 63 percent decrease in mortality. Over a million early deaths are averted every year because of the research of the past 30 years. Economists tell us that this is worth \$2.6 trillion in economic return because a cohort of individuals who would have died in their 50s now do not and then can produce economic return. We have enormously exciting, effective strategies for not only curing, but preventing and ultimately eliminating coronary heart disease.

Now, you may ask yourself, what was the investment that the American people, that each one of us made to achieve that? Well, over the past 30 years each one of us has spent about \$3.70 per year for medical research related to coronary heart disease. If you look at the total cumulative total over 30 years for heart research, it is \$110 per person. I submit to you that medical research has delivered, for an investment that I think is extremely effective in its return.

Cancer is another example. If you look at cancer—and you mentioned the war on cancer, Senator—for the first time in recorded history, this year we have a lower number of deaths from cancer in the United States, despite an increasing population and an increasing average age of the population. We have 10 million survivors. This is due to the advent of early screening, early detection, new therapies.

What has this cost us? \$8.60 per person per year over the past 30 years. The total investment for each one of us is \$260 over 30 years. I do not think there is an investment that I can describe that any agency can be as proud of as the National Institutes of Health is of its effectiveness. We have delivered not only better cures, but also a healthier life for Americans, who live now longer and healthier lives, with a disability rate that has dropped by 30 percent over the past 22 years because of improvements in bone health, in heart health, and many other advances.

Since 1982 the disability rates have dropped by 30 percent and in the past 30 years American life expectancy has increased by over 6 years, from a total investment cumulative over 30 years, of about \$1,300 per American.

This is not just what we have done in the past. We continue to deliver. If you look at just the advances of the past year—I am just going to take a few examples. If you look at the impact of the

human genome and genomics, we identified over 20 genes just in the past 12 months that relate to prostate cancer and the causes of prostate cancer, in mental health about obsessive compulsive disorder, and one of the most exciting ones is in vision disease, where we have found genes that may explain over 70 percent of cases of what we call age-related macular degeneration, the fastest rising cause of blindness in American seniors.

Vaccines: We have the first global candidate vaccine on HIV/AIDS, that Dr. Fauci and his team developed. Yesterday the FDA approved the first preemptive cancer vaccine against cervical cancer. We have expanded the Avian Flu trials. We have one vaccine in trial and a second one in development. This would not have been possible without the support of Congress and your support here on this committee.

But we realize that biomedical research must continue to deliver and we have a challenge in front of us. We all know that the rising cost of health care and the burden of disease is going to be a challenge for all of us. We see the curve. We see that it is not sustainable. Society spends about \$7,100 per American per year on health care costs. The total NIH spending, \$95 per American per year, has to do something, must do something, to change that picture.

This is the vision of NIH. Our vision, all of us as scientists at NIH, is to use our investment and deliver a complete transformation of medicine, because if we keep practicing medicine the way we know it today, 25 years from now it just will not be sustainable. So discoveries and new ways of not only curing disease, but preventing disease, preempting disease altogether, is the key.

We will do this through what we call the four P's of medicine. It will be more predictive because of our understanding of molecular events. It will be more personalized because we know that every one of us reacts differently to different diseases. It will have to be increasingly preemptive because this is where it is the least costly. But we cannot do this without the participation of everyone, and this is why we say the fourth P is, in the context of chronic diseases like diabetes or obesity, it will require us to include the patients as partners in this new medicine.

PREPARED STATEMENTS

So my message is very simple. We have delivered, we continue to deliver, and we will deliver, and the return on investment is in my view one of the most remarkable returns that anyone can describe, and we will continue to do so. I am happy to take any questions.

[The statements follow:]

PREPARED STATEMENT OF DR. ELIAS A. ZERHOUNI

Mr. Chairman and distinguished members of the subcommittee, it is an honor and a privilege to appear before you today to present the National Institutes of Health (NIH) budget request for fiscal year 2007 and discuss the priorities of NIH for this year and beyond.

BUDGET REQUEST

The request for NIH is \$28.4 billion in fiscal year 2007, the same as the fiscal year 2006 level for the Agency. The budget request will support the research programs managed by NIH's Institutes and Centers. At this budget level, NIH will in-

crease the biodefense research program by \$110 million for Advanced Development. Support for the Pandemic Influenza Preparedness Plan will increase by \$17 million. We have also chosen to carefully invest in several trans-NIH strategic initiatives. The NIH Roadmap, an incubator for new ideas and initiatives that will accelerate the pace of discovery, increases by \$113 million. We allocated \$40 million to the Institutes and Centers to launch the Genes, Environment and Health Initiative to accelerate discovery of the major genetic and environmental factors for diseases that have a substantial public health impact. We have also directed \$15 million to the new "Pathway to Independence" program to increase our support of new investigators.

I will focus my testimony on the return of the investment in NIH for the American people. In particular, I will discuss how discoveries fueled by this investment are transforming the practice of medicine. We can now clearly envision an era when the treatment paradigm of medicine will increasingly become more predictive, personalized and preemptive. We will strike disease before it strikes us with the hope of greatly reducing overall costs to society. We expect to move away from the costly and predominantly curative model of today, which requires us to wait for the disease to occur before intervening. I will share with you the strategic vision of NIH and discuss the many management innovations we have implemented to ensure optimal stewardship of taxpayers' resources.

SELECTED ACCOMPLISHMENTS OF NIH AND THEIR IMPACT ON HEALTH

The achievements of NIH and our private sector partners in medical research are difficult to overstate. According to the latest report on the Nation's health from the Centers for Disease Control and Prevention (CDC), life expectancy continues to rise, now at an unprecedented 78 years for the total U.S. population. Since 1950, the age-adjusted death rate for the total population declined by a remarkable 43 percent. Life expectancy has increased by one year in every five for the past 30 years. Americans are not only living longer, they are healthier. For instance, the disability rate of American seniors dropped by almost 30 percent in the past 20 years, owing to a range of scientific advances.

The following are samples of the many advances driven by the investment in NIH.

ADVANCES IN CARDIOVASCULAR DISEASE AND STROKE

Thirty years ago, it was common for a man or woman to suddenly die of a heart attack or stroke between the ages of 50 and 60. Had this trend continued unabated, today more than 1.6 million lives would have been lost per year. Fortunately, today the toll is much less. The death rates from cardiovascular disease have declined by 63 percent and by 70 percent for stroke. Were it not for the ground-breaking research on the causes and treatment of heart disease, supported in large part by NIH, including recent developments such as drug coated stents, safe levels of blood pressure and cholesterol lowering therapies, heart attacks would still account for 1.2 to 1.3 million deaths per year instead of the actual 515,000 deaths experienced today. The estimated total cumulative investment in cardiovascular research at the NIH per American over the past 30 years, including the doubling period, is about \$110, or about \$4 for each American per year over the entire period.

ADVANCES IN CANCER

The mortality rates of cancer, the second leading cause of death in the United States, have been falling for several years, and this year, for the first time in history, the absolute number of cancer deaths in the United States has decreased. More effective therapies have led to improved outcomes for more than 10 million American cancer survivors. With the increase in budgets between 1999 and 2003, the National Cancer Institute has stimulated a paradigm shift in cancer therapy. We are seeing the emergence of targeted therapies, with the unprecedented ability to use specific molecular targeting to treat tumors with novel agents. We can also detect and treat cancer at earlier stages. The National Cancer Institute's (NCI) Early Detection Research Network (EDRN), launched in 1999, has identified a number of biomarkers that allow for the earlier detection of breast, prostate, colon, lung and other cancers. This year, NCI, in collaboration with the Human Genome Research Institute, has launched a cancer genome pilot project to help further our understanding of the basic biology of cancer and identify additional treatment targets. The estimated total cumulative investment at the NCI per American over the past 30 years, including the doubling period, is about \$258, or about \$9 per American per year over the entire period.

ADVANCES IN HIV/AIDS

Without the development and testing of antiretroviral drugs, there would be no hope for patients with HIV/AIDS. The development of Highly Active Antiretroviral Therapies primarily resulted from the work of a large cadre of NIH-supported scientists and their counterparts in the pharmaceutical industry. Their discoveries about the cellular mechanisms of the disease have transformed AIDS into a manageable disease, preventing hundreds of thousands of hospitalizations and early deaths. To date, 21 antiretroviral drugs and 4 combination formulations have been approved by the FDA. Many more less toxic AIDS drugs are currently in development. Today, fewer than 50 HIV-infected babies are born each year in the United States, sparing 16,000 to 20,000 children from AIDS through the use of antiretroviral drugs to prevent mother-to-child transmission. Mother-to-child transmission rates in developing countries have declined by 40 percent with the use of drug therapy. With the introduction of these new drugs, economists estimate the aggregate potential value of improved survival has been nearly \$400 billion for those infected through 2000. They estimate the aggregate potential value for all past and future cohorts of individuals infected with HIV is almost \$1.4 trillion.

With the additional resources provided during the doubling of the NIH budget, we launched the Vaccine Production Program (VPP) Laboratory to efficiently translate candidate research vaccines, including HIV vaccines, into useable products. Since its inception in 2001, this program has overseen the manufacture of over 29 bulk pharmaceutical compounds formulated into 14 different vaccine products for HIV, as well as West Nile, SARS and Ebola Virus, and expanded our network of clinical trial sites across the globe. This program is enabling NIH to serve the needs of the American people in an age of global risks of infectious diseases.

ADVANCES AGAINST THE THREAT OF PANDEMIC INFLUENZA

Thanks to fundamental advances in viral genomics and genetic engineering, NIH has been able to help in the development of countermeasures against both seasonal and pandemic influenza viruses. We now have a vaccine against the H5N1 virus and will develop a second one in conjunction with CDC. Without such a vaccine, and others under development and testing, we would be completely defenseless against the potential pandemic that threatens the entire world. We are investing in research and development to hasten the production process by converting from egg-based to cell culture-based vaccines. We are developing novel vaccine approaches using a variety of molecular biological techniques, and we launched discovery efforts for new anti-viral compounds against pandemic flu. We initiated a project to identify the genomes of thousands of human and avian influenza viruses, and, to date, 831 influenza genome sequences from human isolates have been deposited in NIH's GenBank, allowing researchers across the world to better understand influenza viruses and develop countermeasures.

DEVELOPMENT OF BIODEFENSE RESEARCH

Since 2001, NIH has directed more than \$10 billion toward protecting the American public from bioterrorism. The 2001 intentional release of anthrax underscored the reality of a bioterrorism threat posed by other Category A agents such as smallpox, plague, tularemia, hemorrhagic fevers, and botulinum toxin. NIH responded swiftly. Promising vaccine candidates for Ebola and smallpox are currently in clinical trials. Identification of the three-dimensional structure of the anthrax toxin complex is fueling the search for compounds that block the toxin's effects, and the discovery of the key mechanism of Ebola virus cell entry prompted experiments demonstrating that Ebola infection could be blocked in laboratory tests. We continue to build a national biodefense research infrastructure that will position the Nation to respond even more quickly and precisely to bioterrorism.

ADVANCES IN DIABETES AND RELATED ILLNESSES

Nearly 21 million Americans have diabetes, a disease that can cause damage to multiple organs and lead to death. Without NIH research, the improvements of the past two decades in the therapies for diabetes would not have occurred. Through large prospective trials, made possible by the doubling of our budget, we have assessed the relative value of drug based approaches versus weight loss and physical activity, and showed it is possible to reduce the risk of type 2 diabetes by 58 percent with lifestyle modifications alone.

Diabetes can also result in vision loss. Four million American adults suffer from diabetic retinopathy, the outcome of damage to the tiny blood vessels in the light-sensitive retina lining the inside of the eye. Nearly a million have the advanced vi-

sion-threatening stage of the disease. The National Eye Institute completed a series of landmark clinical trials to develop novel treatments for diabetic retinopathy. Without these new treatments, 450,000 patients who have advanced disease today would otherwise likely be blind in 5 years. As a consequence, of those currently at risk, only 27,000 would progress to legal blindness, and only 9,000 would become blind today. In addition to reduced suffering and disability, the economic savings from these treatments will reach as much as \$1.6 billion per year.

As another example of payoff from recent NIH research, end-stage renal disease (ESRD)—kidney failure requiring dialysis or transplantation, a complication of diabetes and high blood pressure—results in direct federal expenditures of approximately \$20 billion per year. Through the 1980s and 1990s, the incidence of ESRD nearly doubled each decade, but in the last five years overall rates have stabilized—and even declined in certain population groups. This improvement has been driven by monitoring for proteins in urine to prevent kidney disease or detect it in its early stages. Compared with earlier projections, the savings in federal health care expenditures are approximately \$1 billion dollars per year.

Without the investment in medical research, people with diabetes would be living shorter, less productive, and less hopeful lives.

ADVANCES IN IMAGE-GUIDED MICROSURGERY

Increases in the NIH budget allowed new investments in the use of imaging technologies like CAT scanning, MRI or ultrasonography for the development of new microsurgical techniques. These minimally invasive therapies are changing the fate of many patients, including patients with Parkinson's disease, through deep brain stimulation. These new techniques are also promising to revolutionize the treatment of epilepsy, a disease that affects over 2.7 million Americans. As we move forward with such research, we expect that surgery will become less invasive, more precise and less dangerous, with far less operative complications.

ADVANCES IN HEALTH INFORMATION FOR SCIENTISTS AND THE PUBLIC

The National Library of Medicine of the NIH provides the American public with high quality, reliable information. The NIH web sites (www.nih.gov) are now recognized by independent organizations as the most successful health related web sites, with over 2 million queries per day. Millions of patients and their families regularly consult NIH web sites for up to date information in English and Spanish, a capability made entirely possible by the doubling of the NIH budget. The web-based ClinicalTrials.gov represents a landmark effort to provide information to patients and physicians across the country on NIH-funded clinical trials.

NIH also leads the research field in developing information technology for biomedical research. No biomedical scientist develops a project without first consulting the suite of powerful informational research tools available through the NIH National Library of Medicine's PubMed, a growing digital archive of peer-reviewed research articles and scientific databases.

NEW RESEARCH TOOLS

NIH researchers have pioneered powerful new research tools and methods such as high throughput DNA sequencing, protein identification with mass spectrometry, gene expression arrays, the determination of thousands of new protein structures, and imaging technologies which were simply unavailable before the doubling of the NIH budget. A great illustration of the impact of these advances has been the identification of the cause of the SARS virus in less than a month and the current tracking of pandemic flu viruses. These tools have greatly accelerated the research process itself, spurred progress and spawned new discoveries in all areas of biomedical research. Perhaps nowhere else have these technological advances in imaging and genotyping elicited more excitement than in the field of mental and behavioral health, elucidating genes linked to schizophrenia, depression, bipolar disorder and anxiety. These discoveries are allowing for the first time direct visualization of brain structure and function to study the brain circuitry involved in thinking and a range of behaviors.

NEW DIAGNOSTIC AND THERAPEUTIC TECHNOLOGIES

Some of NIH's successes can be measured in new medical technologies. Advances in research are driving an increase in the number of technologies being licensed to companies for commercialization. In fiscal year 2004, there were thousands of active licenses between federally funded research institutions and companies worldwide. Out of these technologies, several thousand companies are making many new prod-

ucts that have an immeasurable impact on public health. Today, from NIH funded research, more than 300 new drug products and vaccines targeting more than 200 diseases—including various cancers, Alzheimer’s disease, heart disease, diabetes, multiple sclerosis, AIDS and arthritis—are in clinical trials. These outcomes are accomplished through the on-going network of successful collaborations with our colleagues in private industry.

THE CHANGING LANDSCAPE OF DISEASE

Disease and injury are constant threats to humankind and are never static. New diseases can emerge at any time, such as HIV/AIDS, SARS, Pandemic Flu, obesity or many other conditions. Bioterrorism did not figure significantly in the NIH agenda in 2001, but is now a top priority of the agency. Twenty years ago the impact of Alzheimer’s disease was not fully appreciated, nor were its causes known.

As the result of our success in preventing and treating acute and short term conditions such as heart attacks, stroke, cancer and many infectious diseases, we are living longer. Our increasingly older population faces the new challenge of multiple chronic conditions which now consume about 75 percent of healthcare expenditures. This shifting burden of health care from acute to chronic diseases is perhaps the greatest challenge we face.

Health care costs in the United States have risen to more than \$2 trillion. The amount spent on health care per person has doubled, from \$3,461 in 1993 to \$7,110 today. The causes of health care inflation are varied and complex, requiring different, nation-wide solutions.

We are in a race against the overwhelming human and economic consequences of disease. We can win this race, but only if we use research discoveries to transform medicine as we know it. Thanks to recent research advances, we can foresee a future of more effective medical treatment that might be less expensive than current practices.

STRATEGIC VISION FOR NIH: FROM CURATIVE TO PREEMPTIVE CARE

We are in an era of great scientific opportunity. Advances in our understanding of basic human biology allowed NIH to sequence the human genome by 2003, two years ahead of schedule, and to complete the Haplotype Map, showing the variation between individual humans, in October 2005, also ahead of plans. One of the greatest scientific achievements in history, the genome blueprint, along with work in systems biology and proteomics, are driving a revolutionary period in the life sciences. We are on the brink of transforming medical treatment in the 21st Century. Our hope is to usher in an era where medicine will be predictive, personalized and preemptive.

Toward this goal, NIH is strategically investing in research to further our understanding of the fundamental causes of diseases at their earliest molecular stages so that we can reliably predict how and when a disease will develop and in whom. Because we now know that individuals respond differently to environmental changes according to their genetic endowment and their own behavioral responses, we can envision the ability to precisely target treatment on a personalized basis. Ultimately, this individualized approach, completely different than how we treat patients today, will allow us to preempt disease before it occurs.

Consider, for instance, how better predictive and personalized treatments could improve the safety and effectiveness of drugs. As we know, drugs do not fall into the “one size fits all” category. The same drug can help one patient and harm another. Recent research shows that we will be increasingly able to know which patients will benefit from treatment and which patients might be harmed. This field of study is known as pharmacogenetics. Using the latest genomic data, enabled by the doubling of the NIH budget, the NIH established a Pharmacogenetic Research Network which is studying the interactions of drugs and molecules as well as the biological processes that eliminate compounds from the body. In the first five years of this program, the researchers in this network made numerous discoveries.

For example, they learned that 10 percent of the North American population exhibits a genetic variation that puts them at high risk for life-threatening reactions to irinotecan, a cancer drug. We now know that patients with this variation should be given lower than prescribed doses of this successful drug, thus potentially saving their lives.

NIH researchers also discovered variations in a gene involved in the body’s response to more than half of all medications. Understanding these differences could explain critical individual as well as racial and ethnic differences in drug responses. Other genetic variations discovered by the NIH network will have an impact on

asthma treatment, the risk of sudden death from irregular heartbeats and the proper use of blood thinning medications to avoid deadly bleeding complications.

In another example of emerging personalized medicine, cancer researchers have developed a test that helps determine the risk of recurrence for women who were treated for early stage, estrogen-dependent breast cancer. This information can help a woman and her doctor decide whether she should receive chemotherapy in addition to standard hormonal therapy. This test has the potential to change medical practice by sparing tens of thousands of women each year the unnecessary and harmful side effects associated with chemotherapy at large potential cost savings.

RAPID ADVANCES IN THE GENOMIC ERA

Because of a hundred fold reduction in the cost of genomic technology, we can now study, at affordable costs, the differences between patients who have a disease and their normal counterparts. Recently, this revolutionary approach led to the discovery of two previously unsuspected factors that can identify who is at risk and how to protect patients from age-related macular degeneration, an increasing cause of blindness in our aging population, with over 7 million Americans at risk. Last month, a key transcription factor that may be responsible for a large percentage of cases of diabetes was discovered.

These breakthroughs form the basis of our budget request for the Genes and Environment Initiative, supported by Secretary of Health and Human Services Michael Leavitt, because it will give us the unprecedented ability to discover, over the next three years, the potential causes of the 10 most common diseases afflicting the U.S. population. With this funding, if approved, we will also launch a technology development effort for enabling scientists to measure many types of environmental exposures at the individual level. Taken together, these efforts will lead to better understanding of the environmental and genetic factors in the development of many diseases.

Imagine a world where we will be able to tell each patient whether they need to take action to preempt altogether the development of costly and painful diseases. Imagine telling them that they do not need to take expensive medications for life because they are not at risk of disease. A more predictive, personalized and preemptive form of medicine is no longer just a dream, but a vision to strive for as rapidly as we can.

MANAGEMENT INNOVATIONS

NIH has an enormous and growing scope of mission. We conduct or support research on over 6,600 diseases and conditions, from the most common to the rarest. In 2005, more than 43,000 research grant applications went through our rigorous two-tiered review process, with about 22 percent of applications ultimately receiving funding.

More than 80 percent of the NIH budget supports extramural research at 3,100 institutions around the world, employing about 200,000 scientists and other research personnel. Another 10 percent of the budget goes into the NIH intramural program, consisting of approximately 6,000 scientists, where work is focused on public health priorities and cutting edge research. The hub of the intramural program, the NIH Clinical Center on the Bethesda campus, is the world's largest dedicated clinical research complex.

NIH is spending \$95 per American this year on medical research, and we need to make every dollar count. With the growth and increasing complexity of the agency, NIH has aggressively moved to transform its management strategies and decision-making processes. To streamline, harmonize and better coordinate decisions that affect the entire agency, in 2003, I established the NIH Steering Committee, composed of nine Institute Directors who serve on a rotating basis. Six working groups support the Steering Committee. This new governance structure has enabled greater coordination and harmonization between the 27 Institutes and Centers at NIH.

NIH has addressed the need for more robust means to oversee the vast NIH research portfolio, and plan and launch trans-NIH initiatives. While the NIH successfully developed important trans-NIH initiatives such as the Roadmap for Medical Research, the Strategic Plan for Obesity Research, and the Neuroscience Blueprint, the agency is now implementing even more rigorous and transparent processes and developing cutting-edge tools to analyze, assess and manage the array of research it supports. This will provide better information to support planning and priority-setting in areas of shared Institute and Center interests. To reinforce these accomplishments, NIH is establishing a new office within the Office of the Director—the Office of Portfolio Analysis and Strategic Initiatives (OPASI).

Review of our programs by the Office of Management and Budget under the congressionally mandated Government Performance and Results Act (GPRA) provides evidence that our programs are effective. We have been rated in the top 15 percent of federal organizations.

NIH's effective performance is reflected in recent scores as measured by the OMB Program Assessment Rating Tool (PART). In the fiscal year 2007 PART, the Buildings and Facilities Program and the Intramural Research Program both received the highest possible rating of effective, with scores of 96 percent and 90 percent, respectively. On the fiscal year 2006 PART, the NIH Extramural Research Program achieved a similarly high 89 percent. These high scores demonstrate exemplary management and substantial progress toward meeting NIH performance measures. To date, approximately 90 percent of NIH's budget has been PARTed and rated effective.

TRANSLATING DISCOVERIES INTO BETTER MEDICAL TREATMENT

Rapidly translating our discoveries from the bench to the bedside is a top priority of the NIH. The opportunities have never been greater to use modern research methodologies such as genomics, proteomics, metabolomics, high sensitivity biochemical methods and other novel strategies to bring new insights to the study of human populations and more rapidly achieve the goal of making medicine predictive, personalized and preemptive.

To accelerate progress, NIH recently introduced the institutional Clinical and Translational Science Award (CTSA). The CTSA program will stimulate institutions across the country in transforming Clinical and Translational Science in the U.S.A. to (1) captivate, advance, and nurture a cadre of well-trained multi- and inter-disciplinary investigators and research teams; (2) create an incubator for innovative research tools and information technologies; (3) synergize multi- and inter-disciplinary clinical and translational research; and (4) accelerate the application of new knowledge and techniques to clinical practice at the front lines of patient care.

TRAINING A NEW GENERATION OF SCIENTISTS

New visions require new talent. In times of constrained budgets the most important action NIH needs to take is to preserve the ability of young scientists with fresh ideas to enter the competitive world of NIH funding. To that effect, NIH has launched the new "Pathway to Independence" program which will support, for each of the next five years, 150 to 200 recently trained scientists conducting independent, innovative research.

IN SUMMARY

Our Nation's investment in biomedical research has dramatically improved health outcomes. The return on the investment of the American people at NIH is nothing short of spectacular. Thanks to the support of Congress, we are able, through our science, to respond in record time to emerging threats such as SARS, Pandemic Flu and biodefense needs. We have learned how to decrease the incidence of many diseases and other disabilities for old and young Americans. The estimated total cumulative investment at the NIH per American over the past 30 years including the doubling period is about \$1,334 or about \$44 per American per year over the entire period. In return, Americans have gained over six years of life expectancy and are aging healthier than ever before.

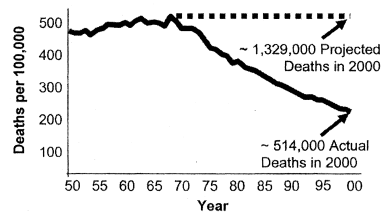
The President and Congress have wisely invested in biomedical research. We are acutely aware that NIH research is often the only hope for millions of people afflicted by disease. In the battle for health, NIH also believes that it needs to accelerate the pace of progress, as it is only through a fundamental transformation of medicine that solutions to the rising burden of healthcare will be found.

I will be happy to answer any questions you may have.

- What is the return on the American people's investment in the National Institutes of Health?
- What has the NIH budget doubling delivered?
- What is the NIH strategy for the future?



Biomedical Research Has Delivered *Coronary Heart Disease*

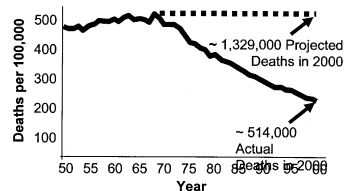


- 63% decrease in Mortality
- ~ 1 million early deaths averted per year
- \$2.6 trillion in economic return
- New, effective treatments and prevention strategies



Biomedical Research Has Delivered Coronary Heart Disease

Average investment
per American
~\$3.70
per year

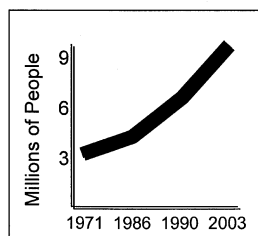
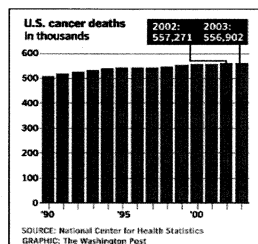


30-year investment
per American:
~\$110
Total

- 63% decrease in Mortality
- ~ 1 million early deaths averted per year
- \$2.6 trillion in economic return
- New, effective treatments and prevention strategies



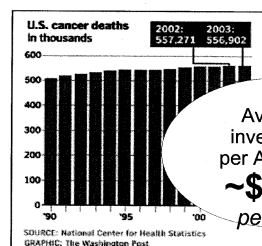
Biomedical Research Has Delivered Cancer



- For the first time in recorded history, annual cancer deaths in the United States have fallen
- 10 million survivors
- Advent of early detection and screening



Biomedical Research Has Delivered *Cancer*

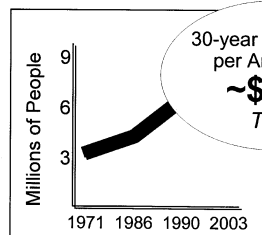


Average
investment
per American
~\$8.60
per year

■ For the first time in recorded history, annual cancer deaths in the United States have fallen

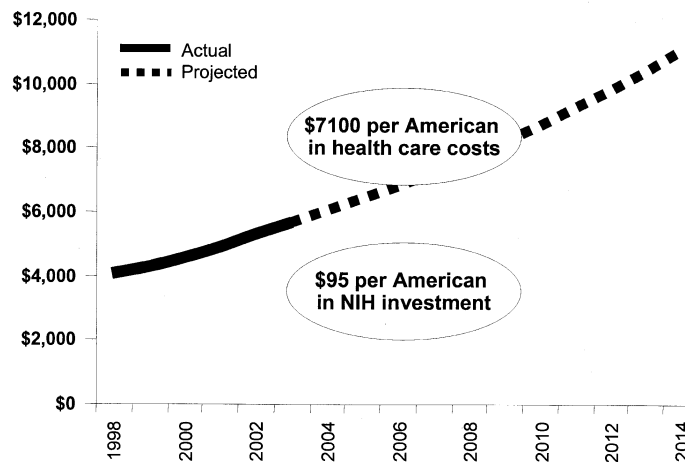
■ 10 million survivors

■ Advent of early detection and screening



Facing the Rising Challenge

U.S. Health Expenditures per capita



Source: <http://new.cms.hhs.gov/NationalHealthExpendData/downloads/nheprojections2004-2014.pdf>

Biomedical Research Has Delivered

Americans Live Longer, Healthier Lives



■Improvements in:

- Recovery from heart disease, stroke
- Deafness
- Vision impairment
- Osteoporosis
- Arthritis



Biomedical Research Has Delivered

Americans Live Longer, Healthier Lives



Since 1982,
disability rate for
elderly Americans
declined by 30%

In past 30 years,
American life
expectancy
increased by ~6
years

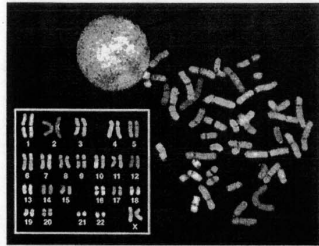
■Improvements in:

- Recovery from heart disease, stroke
- Deafness
- Vision impairment
- Osteoporosis
- Arthritis



Biomedical Research Is Delivering

NIH Advances in the Past Year



■ Genomics:

- Identified >20 genes influencing diseases, including:
 - Prostate Cancer
 - Obsessive Compulsive Disorder
 - Age-related Macular Degeneration

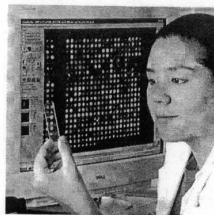
■ Vaccines:

- First “global” HIV/AIDS vaccine
- First Cervical Cancer vaccine
- Expanded Avian Flu vaccine clinical trials



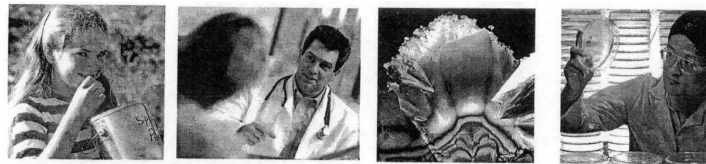
Biomedical Research Will Deliver

Transforming Medicine through Discovery

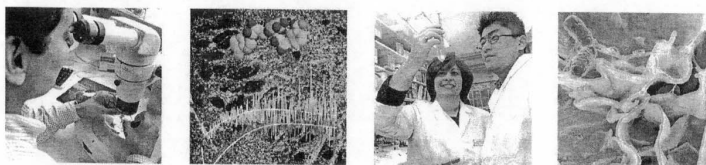


Predictive ↔ Personalized ↔ Preemptive





NIH *Transforming medicine through discovery*



PREPARED STATEMENT OF DR. JOHN E. NIEDERHUBER

Mr. Chairman and Members of the Committee: I am please to present the fiscal year 2007 President's budget request for the National Cancer Institute (NCI). The fiscal year 2007 budget includes \$4,753,609,000, a decrease of \$39,747,000 below the fiscal year 2006 enacted level of \$4,793,356,000 comparable for transfers proposed in the President's request.

OUR GOAL REMAINS THE SAME

Four years ago, we put the NCI on a trajectory towards the Challenge Goal of eliminating suffering and death due to cancer as early as the year 2015. Since that time, we have vigorously and aggressively managed NCI's portfolio of investments in cancer research across that entire continuum of the process of cancer, whether we've been focusing on understanding genetic mutations that were responsible for susceptibility to cancer or focusing on issues that have to do with survivorship and living with, rather than dying from, cancer.

NCI has been a major leader in the molecular metamorphosis of biomedical medicine that has benefited all fields of medical research. Without the Nation's support of NCI's pioneering role in funding research—including basic science, clinical trials, and translational investigations—into the molecular and genetic processes that underlie all disease and the training of new cancer researchers, it is unlikely that the advances we are seeing today in many health areas—from AIDS to macular degeneration—would have occurred at the pace they have. These leadership efforts must be sustained going forward.

The Nation's past commitment to cancer research has proven its worth: mortality rates have declined for all cancers combined while incidence rates have stabilized or increased slightly, detection and treatments have improved, new therapeutic options offer startling promise. Today there are nearly 10 million cancer survivors in the United States compared to approximately 3 million cancer survivors in 1971 when the National Cancer Act was established. Also, in 1971 fewer than half of those found to have cancer lived 5 years beyond their diagnosis; today the 5 year survival rate is 64 percent for adults and 79 percent for children aged 14 or younger. The latter figure is truly remarkable given how few children survived even a couple of years after being diagnosed in the early 1970s. NCI's continued commitment is manifested today in far-reaching programs that have advanced our basic understanding of the genetic changes responsible for this dreaded disease. The Nation's investment and the actions of Congress are directly responsible for the devel-

opment of a nation-wide network of 61 NCI-designated cancer centers and a highly successful Community Clinical Oncology Program (CCOP), founded in 1983. Through the network of 64 CCOP grantees, community investigators participate actively in NCI-sponsored cancer prevention, control, and treatment clinical trials. These programs place cutting-edge research directly in communities and put access to cancer clinical trials into the hands of local physicians. Because of their participation in NCI trials, community clinicians more readily adopt new regimens, ensuring that these advances are rapidly made part of the standard of care.

Recently, NCI's leadership team has initiated a series of site visits to innovative community-based cancer centers as potential models for a new NCI initiative, the Community Cancer Centers Program (CCCCP). The CCCC would help foster replication of successful community models across the country, set the standards for multi-specialty state-of-the-art care, provide access to early phase clinical trials, and ultimately improve cancer care and outcomes. This program is especially designed to bring academic standards of care and clinical trials directly to the segments of our population who either through age or resources cannot leave their community.

A RECORD OF REAL SUCCESS

The past year in cancer research shows a record of substantial and heartening achievement. We are expanding our foundation of knowledge and the technical tools with which rapid advances can be made in understanding the mechanisms of cancer. We are exponentially increasing the opportunities to manage this lethal disease. Building on NCI-funded research, large-scale clinical trials in 2005 yielded results that will have profound effects in preventing and treating many cancers.

For example, three different clinical trials showed that adding trastuzumab (Herceptin®) to standard adjuvant chemotherapy significantly reduced the risk of recurrence in women with the early-stage breast cancer, HER-2/neu positive, which has an over expression of protein in the gene. Approximately 50,000 women in the United States are diagnosed with HER-2/neu positive breast cancer each year, representing about 20 percent of invasive breast cancers.

Equally stunning results were seen in the trial of a vaccine that protects against two strains of human papillomavirus (HPV) that cause over 70 percent of cervical cancers, a disease that kills more than 200,000 women each year, including many in developing countries. Study results concluded that women who received the vaccine during a 2-year study were protected against precancerous lesions caused by HPV. NCI made the initial discoveries linking HPV to cervical cancer, which led to creation and testing of HPV vaccines that are based on technology also developed at the Institute. It is an outstanding exemplar in this era of molecular medicine of how NCI's knowledge about the etiology of the disease enabled creation of a vaccine against a specific cancer.

In January, an NCI-sponsored trial reported that women who received chemotherapy directly in their abdomens as part of treatment for advanced ovarian cancer lived more than a year longer than women who received the same chemotherapy intravenously. The findings confirm and expand recent research showing that intraperitoneal (IP) chemotherapy, which delivers drugs directly to the abdominal cavity through a catheter, can significantly increase survival for some women with the disease. As the results were made public, NCI issued a rare clinical announcement to raise awareness about IP chemotherapy for ovarian cancer among physicians and patients. The NCI announcement—the first since 1999—was warranted because IP chemotherapy is widely regarded as an old technology and previous trials have generated little interest among physicians. Ovarian cancer causes the most deaths of any gynecological cancer in the United States and frequently goes undetected until tumors spread beyond the ovaries.

Another notable advance came last September with the announcement of results from the NCI-sponsored Digital Mammographic Imaging Screening Trial (DMIST). The study found that digital mammography is more accurate than film mammography for women with dense breasts, as well as for several other groups of women, including women under 50 and pre- and perimenopausal women. Overall, DMIST offers a model case study of how NCI can be an agent of change, pursuing new approaches to research, partnering with the private and public sectors, and fueling the development of technologies to achieve an important advance. It is particularly noteworthy that NCI and the American College of Radiology Imaging Network (ACRIN) secured the involvement in DMIST of four companies that developed and manufactured digital mammography machines for our use in clinical trials: Fischer Medical, Fuji Medical, General Electric Medical Systems, and Hologic.

Finally, NCI has made strides to address the widespread disparities in cancer screening, treatment, and care for disadvantaged, mostly minority populations. One

approach to closing this access gap is NCI's Patient Navigator Research Program, which relies on personal guides to shepherd disadvantaged cancer patients into standard care. NCI supports a number of Patient Navigator Program pilot projects in minority communities and about \$24 million in grants will be awarded over the next 5 years as part of the program.

ADVANCED TECHNOLOGIES ACCELERATE PROGRESS

The technology revolution is speeding up and enabling the discovery process. Nanotechnology has emerged as a key strategy for imaging molecular features of cancer and will ultimately lead to personalized medicine. NCI's investment in nanotechnology is a powerful example of leveraging resources from the private sector through our Centers of Cancer Nanotechnology Excellence.

Of equal significance, in December 2005 NCI and the National Human Genome Research Institute (NHGRI) launched The Cancer Genome Atlas (TCGA) Pilot Project, a comprehensive effort to accelerate understanding of the molecular basis of cancer and which evolved from the Human Genome Project (HGP). The TCGA Pilot Project will develop and test the science and technology needed to systematically identify the genetic changes in a small number of cancers.

Additionally, NCI's cancer Biomedical Informatics Grid (caBIG™) is creating a unifying technology platform or "world-wide web" for cancer research. caBIG™ is well on the way to its goal to create a network of interconnected data, applications, individuals, and institutions that will redefine how cancer research is conducted and care is provided. This initiative has also whetted considerable commercial interest.

INTERAGENCY COLLABORATIONS

Addressing the cancer problem requires that NCI work across institutional and sector boundaries, share knowledge, and bring together the diverse members of the Department of Health and Human Services (DHHS) family of agencies, as well as other federal offices, that can help develop systems-based solutions to the cancer problem.

The NCI and FDA Interagency Oncology Task Force (IOTF) continues to remove bottlenecks in the process of developing and approving safe, more effective cancer interventions. During 2005, IOTF helped foster the creation of two important initiatives: the Exploratory Investigational New Drug (IND) process to streamline the early clinical development of new drugs and biologics; and the NCI Regulatory Affairs Liaison position to help NCI-funded researchers navigate through FDA's IND application process. Both will help eliminate obstacles to the rapid development of promising new anticancer agents.

DHHS Secretary Mike Leavitt announced last month the Oncology Biomarker Qualification Initiative (OBQI)—an unprecedented interagency agreement among NCI, FDA, and the Centers for Medicare and Medicaid Services (CMS) to collaborate on improving the development of cancer therapies and the outcomes for cancer patients through biomarker development and evaluation.

CONCLUSION

We must do more to continue the acceleration of discovery, development, and delivery of the interventions that will hasten the transformation of our traditional view of cancer as a death sentence into a disease that we can prevent, eliminate, or control. This will be the legacy we leave our children.

While progress is evident, there is much that remains to be accomplished. We are committed to face the challenge of making difficult choices between those programs that we will continue to grow and nurture and those that have already advanced our knowledge. The decisions will be science driven. This is an unprecedented era of discovery. The opportunities to apply powerful new technologies to advance our knowledge and the opportunities to change the course of cancer have never been greater.

PREPARED STATEMENT OF DR. FRANCIS S. COLLINS

Mr. Chairman and Members of the Committee: I am pleased to present the fiscal year 2007 President's budget request for the National Human Genome Research Institute (NHGRI). The fiscal year 2007 budget includes \$482,942,000, a decrease of \$3,107,000 from the fiscal year 2006 enacted level of \$486,049,000 comparable for transfers proposed in the President's request.

On October 26, 2005, an international consortium of dedicated scientists from six countries, led by the NHGRI, published a new map of the human genome called

“HapMap” that may prove even more powerful than the human genome sequence because of its medical applications.

The Human Genome Project (HGP) spelled out the letters of the 99.9 percent of the DNA code that we all share. The haplotype map, or HapMap for short, provides detailed knowledge of the 0.1 percent that represents variation in the genome. The HapMap reveals the way in which this genetic variation is organized into chromosomal neighborhoods and provides a powerful tool to uncover those spelling differences in the human instruction book that predispose some people to diabetes, Alzheimer’s disease, heart disease, or cancer. As with the HGP, all of the data has been placed in the public domain.

Since early deliberations about the HGP 20 years ago, scientists and physicians have dreamed of the day when we would be able to apply the tools of genomics to the diagnosis, treatment, and prevention of those common diseases that fill up our hospitals and clinics, causing untold suffering, misery, and premature death. The completion of the HapMap brings us a major step closer to the realization of that dream.

The HapMap project could not have succeeded without the support of multiple NIH institutes, the U.S. Congress, and the dedication of more than 2,000 scientists across the world who delivered on every promise of the project. In fact, in its brief three-year life, this project produced a map three times more detailed than originally thought possible. The NHGRI and other NIH institutes can now move quickly to build on this success to discover the genetic and environmental factors that cause disease, and to utilize this information to develop better means of individualized prevention and treatment.

ONGOING NHGRI INITIATIVES

Use of Comparative Genomics to Understand the Human Genome

The NHGRI continues to support the sequencing of the genomes of non-human species such as the chimpanzee, dog, and mouse because of what they tell us about the human genome. The first comprehensive comparison of the genetic blueprints of humans and chimpanzees, published in *Nature* to wide acclaim in September 2005, shows our closest living non-human relatives share identity with 96 percent of the human DNA sequence. The sequence of the dog genome was published in December 2005, revealing many interesting details about the remarkable diversity of man’s best friend, and greatly empowering the ability to track down the genes involved in many chronic illnesses (like cancer) where dogs are excellent models for human disease.

Sequencing technology advances, on the way to the \$1,000 genome

DNA sequencing enables a detailed description of the order of the chemical building blocks, or bases, in a given stretch of DNA, and is a powerful engine for biomedical research. Though DNA sequencing costs have dropped by three orders of magnitude since the start of the HGP, sequencing an individual’s complete genome for medical purposes is still prohibitively expensive. Two bold new advances in sequencing technology recently developed by NHGRI-funded researchers promise to greatly reduce this cost. Ultimately, the NHGRI’s vision is to cut the cost of whole-genome sequencing to \$1,000 or less. If achieved, this would enable the sequencing of individual genomes as part of routine medical care, providing health care professionals with a more accurate means to predict disease, personalize treatment, and preempt the occurrence of illness.

Knockout Mouse Project

The technology to “knockout” or inactivate genes in mouse embryonic stem cells has led to many insights into human biology and disease. However, information about knockout mice have only been published and made available to the research community for about 10 percent of the estimated 20,000 mouse genes. Recognizing the wealth of information that mouse knockouts can provide, the NHGRI coordinated an international meeting in 2003 to discuss the feasibility of a comprehensive project. These discussions have now resulted in a trans-NIH, coordinated, five-year cooperative research plan that will produce knockout mice for every mouse gene and make these mice available as a community resource.

Chemical Genomics—Roadmap—Molecular Libraries and PubChem

The NHGRI has taken a lead role in developing a trans-NIH chemical genomics initiative. This is part of the NIH Roadmap, and now offers public-sector researchers access to high throughput screening of libraries of small organic compounds that can be used as chemical probes to study the functions of genes, cells, and biochemical pathways. This powerful technology provides novel approaches to explore

the functions of major components of the cells in health and disease. All the data generated for this project is stored in the new PubChem database at the National Library of Medicine.

Bench-to-Bedside in Intramural Research—The Example of Progeria

As just one example of the focus of the NHGRI intramural program on translational research, rapid advances have recently been achieved in the study of progeria, a rare genetic disease of childhood characterized by dramatic acceleration of aging. In 2003, NHGRI researchers discovered that progeria is caused by a single letter misspelling in a gene known as *lamin A*. The *lamin A* protein undergoes a particular modification known as farnesylation. That same modification activates the protein product of the famous ras oncogene; ten years of hard work has made available a class of cancer drugs that blocks this step. Remarkably, cell culture and mouse model experiments suggest these drugs may also have benefits for children with progeria. Serious consideration of a clinical trial is now underway, just three years after gene discovery.

The Surgeon General's Family History Initiative

Family medical history is a source of genetic information that can help more accurately determine an individual's risk for specific diseases. However, to date, this resource has been underutilized in health. To address this, Surgeon General Richard Carmona established the U.S. Surgeon General's Family History Initiative, a collaborative effort between a number of Department of Health and Human Services agencies, with leadership from NHGRI. The second annual National Family History Day was celebrated on Thanksgiving Day 2005, when a new and improved version of the software tool called "My Family Health Portrait" was released to help individuals compile their own family history information. This initiative should have an impact on patient-healthcare provider interaction, facilitating the development of more accurate family history information for patient medical records, and leading to more personalized and effective disease prevention and treatment strategies.

NEW NHGRI INITIATIVES

The Genes and Environment Initiative (GEI) and the Genetic Association Information Network (GAIN).

Just this February, the Department of Health and Human Services announced the creation of two related groundbreaking initiatives in which NHGRI will play a leading role, to speed up research on the causes of common diseases such as asthma, arthritis, the common cancers, diabetes, and Alzheimer's disease.

The Genes and Environment Initiative (GEI) is a trans-NIH research effort to combine comprehensive genetic analysis and environmental technology development to understand the causes of common diseases. NIH will invest \$68 million in GEI in fiscal year 2007. Using the newly derived HapMap, GEI will search for the specific DNA variations that are associated with an increased risk of common illnesses. For the more than a dozen disorders chosen for investigation under GEI, NIH will study roughly 1,000 cases and 1,000 controls will be studied. Finding the variants that predispose a person to common disease is one of the highest priorities of current biomedical research, as this will enable developing personalized medicine and identifying new drug targets.

To ensure that GEI takes advantage of the wide breadth of expertise that is available on DNA variations for common disorders, NIH has begun partnering under the Genetic Association Information Network with the Foundation for the NIH, Pfizer, and Affymetrix to begin research on seven diseases during this fiscal year.

But genes alone do not tell the whole story. Recent increases in chronic diseases like diabetes, childhood asthma, obesity or autism cannot be due to major shifts in the human gene pool as those changes take much more time to occur. They must be due to changes in the environment, including diet and physical activity, which may produce disease in genetically predisposed persons. Therefore, GEI will also invest in innovative new technologies/sensors to measure environmental toxins, dietary intake and physical activity, and using new tools of genomics, proteomics, and understanding metabolism rates to determine an individual's biological response to those influences.

The Cancer Genome Atlas (TCGA)

In December, the National Cancer Cancer Institute (NCI) and the National Human Genome Research Institute (NHGRI) jointly launched a very important new effort to accelerate our understanding of the molecular basis of cancer through the application of genome analysis technologies, including large-scale genome sequencing. Thanks to the tools and technologies developed by the Human Genome Project and

recent advances in using genetic information to improve cancer diagnosis and treatment, it is now possible to envision a comprehensive effort to map the changes in the human genetic blueprint associated with all known forms of cancer. The overall effort, called The Cancer Genome Atlas, will begin in 2006 with a three year, pilot project totaling \$100 million to determine the feasibility of a full-scale effort to explore the universe of genomic changes involved in all types of human cancer. This atlas of genomic changes will provide: (1) new insights into the biological basis of cancer which in turn will lead to new tests to detect cancer in its early, most treatable stages; (2) new ways to predict which cancers will respond to which treatments; (3) new therapies to target cancer at its most vulnerable points; and (4) ultimately, new strategies to prevent cancer altogether.

OTHER AREAS OF INTEREST

Education of Health Care Professionals

To enable the translation of basic genetic discoveries into health care practice, the NHGRI has developed numerous educational programs to prepare health care professionals for this revolution. Specifically, the NHGRI continues to play a lead role in the National Coalition for Health Professional Education in Genetics (NCHPEG), which is leading a national effort to achieve genetic literacy amongst health professionals. NHGRI also worked closely with the American Academy of Family Physicians, who featured genomic medicine as their educational focus for 2005.

Minority Outreach Activities

The NHGRI has been at the forefront of ensuring that minority scientists and students are equipped to meet the new challenges of genome research for the 21st century. The institute has sponsored new initiatives to reach out to diverse populations including research, education, and outreach collaborations on the role of genetic factors in health disparities. In conjunction with the National Council of La Raza, NHGRI has developed a community-based model education program for provision of genetics information to underserved Latino communities. NHGRI is also working with Alaska Native communities and the University of Washington to expand community-based education programs in Alaska Native communities.

Genetic Nondiscrimination

The NHGRI remains very concerned about the impact of potential genetic discrimination on research and clinical practice. Through many surveys and research projects funded by the Ethical, Legal, and Social Implication (ELSI) program of the Institute, it is clear many Americans remain concerned about the possible misuse of their genetic information by insurers or employers. In February 2005, the Senate unanimously passed the Genetic Information Nondiscrimination Act of 2005 (S. 306), which would address these concerns; the companion bill H.R. 1227 is now pending in the House. The Bush Administration has issued a Statement of Administrative Policy in support of the legislation. This issue remains a high priority for the Institute.

PREPARED STATEMENT OF DR. ANTHONY S. FAUCI

Mr. Chairman and Members of the Committee: I am pleased to present the President's budget request for the National Institute of Allergy and Infectious Diseases (NIAID) of the National Institutes of Health (NIH). The fiscal year 2007 budget of \$4,395,496,000 includes an increase of \$12,195,000 over the fiscal year 2006 appropriated level of \$4,383,301,000, comparable for transfers proposed in the President's request.

The mission of NIAID is to conduct and support research to understand, treat, and prevent infectious and immune-related diseases. Infectious diseases include well-known killers such as HIV/AIDS, malaria, and tuberculosis; emerging or re-emerging threats such as influenza; and "deliberately emerging" threats from potential agents of bioterrorism. Immune-related disorders include autoimmune diseases such as type 1 diabetes and rheumatoid arthritis as well as asthma, allergies, and problems associated with transplanted tissues and organs.

NIAID has a two-fold mandate. First, NIAID must plan and execute a comprehensive and long-term basic and clinical research program on well-recognized endemic infectious and immune-mediated diseases. Second, and in this case it is unique among the NIH Institutes, it must respond quickly with targeted research to meet new and unexpected infectious disease threats as they arise, often in the form of public health emergencies. Part of the expansion of the NIAID research portfolio in recent years has been driven by unprecedented scientific opportunities in the core

NIAID scientific disciplines of microbiology and immunology. Advances in these key fields have led to a better understanding of the human immune system and the mechanisms of infectious and immune-mediated diseases. But the scope of NIAID programs also has grown because of a growing realization that biomedical research is a key component of a successful response to new challenges posed by emerging and re-emerging infectious diseases such as pandemic influenza and HIV/AIDS, the threat of bioterrorism, and the increase in asthma prevalence among children.

EMERGING AND RE-EMERGING INFECTIOUS DISEASES

Despite advances in medicine and public health such as antibiotics, vaccines, and improved sanitation, the World Health Organization (WHO) estimates that infectious diseases still account for approximately 26 percent of all deaths worldwide, including about two-thirds of all deaths among children younger than five years of age. Moreover, the pathogens we face are not static, but change dramatically over time as new microbes emerge and familiar ones re-emerge with new properties or in unusual settings.

Influenza is perhaps the most pertinent example of a re-emerging disease. Influenza viruses continually accumulate small changes such that a new vaccine must be made for each influenza season. When a totally new influenza virus against which the global population has no natural immunity emerges, a worldwide pandemic can result if the new viruses are able to transmit efficiently between people. Three such pandemics occurred in the 20th century, in 1918, 1957, and 1968. The pandemics of 1957 and 1968 were severe infectious disease events that killed approximately two million and 700,000 people worldwide, respectively. The 1918–1919 pandemic, however, was catastrophic. Public health experts estimate that the 1918 pandemic killed more than 500,000 people in the United States and more than 50 million people worldwide.

The highly pathogenic H5N1 avian influenza virus currently found in domestic and migratory birds in Asia, Africa, the Middle East, and Europe is of great concern. Although H5N1 is primarily an animal pathogen, it nonetheless has infected more than 170 people; more than half of all confirmed H5N1 patients have died. At this time, the virus is not able to spread efficiently from animals to humans and is extremely inefficient in spreading from person to person, but the feared human influenza pandemic could become a reality if the H5N1 virus mutates further or mixes its genes with human influenza viruses, remains highly virulent, and acquires the capability to spread efficiently from person to person.

It is imperative that we prepare for the possibility that a new influenza virus will emerge to cause a 1918-like pandemic among human beings. It is important to note, however, that our ability to cope with a pandemic—with a sufficient supply of effective vaccines and antiviral drugs, effective infection control, and clear public communication—will to a large extent depend on how well we cope with seasonal influenza. It is clear that we have not yet optimized our preparedness and responsiveness to this recurring disease, which, according to estimates of the Centers for Disease Control and Prevention (CDC), kills an average of about 36,000 people in the United States each year. The serious vaccine shortage that occurred in the 2004/05 influenza season underscored the difficulties we face in annually renewing the influenza vaccine supply, and highlights the pressing need to move toward adoption of newer vaccine manufacturing techniques and other strategies that can improve the surge capacity, flexibility and speed with which vaccines are made.

NIAID supports numerous research projects that lay the foundation for improved influenza vaccine manufacturing methods, new categories of vaccines that work against multiple influenza strains, as well as the next generation of anti-influenza drugs. Some of these are basic research projects intended to increase our understanding of how animal and human influenza viruses replicate, interact with their hosts, stimulate immune responses, and evolve into new strains. Other projects are more targeted, such as a program to screen compounds for antiviral activity against influenza viruses. One particularly important effort is to develop a vaccine that raises immunity to parts of the influenza virus that do not vary from season to season. Not only would such a vaccine provide continued protection over multiple influenza seasons, it might also offer considerable protection against a newly-emerged pandemic influenza virus and thereby substantially improve our preparedness for pandemic threats.

The Department of Health and Human Services (DHHS) Pandemic Influenza Response and Preparedness Plan designates NIAID as the lead agency for research and development efforts related to pandemic influenza. In this capacity, NIAID has developed and is clinically evaluating several candidate H5N1 vaccines, including inactivated and live-attenuated vaccines, as well as other strategies such as recom-

binant subunit and DNA vaccines. The potential benefits of NIAID research to the American public have been clear and immediate. The pre-pandemic H5N1 vaccine that is currently being stockpiled by DHHS was shown in clinical trials by NIAID to be safe and capable of inducing an immune response that would be predictive of being protective against the H5N1 virus. The dose of vaccine required for this protection, however, is high; and current NIAID studies are aimed at enhancing the response to lower doses of the H5N1 vaccine, particularly with the use of adjuvants, which are compounds that have been shown to enhance the immune response to vaccines. NIAID also conducts surveillance for the molecular evolution of influenza viruses among animals and humans in Asia and elsewhere, and tracks changes in the virus that might allow it to be transmitted more easily among people. The Institute also is evaluating new antiviral drugs against H5N1 influenza as well as combinations and varied doses of existing drugs. In addition, NIAID is working to establish a clinical trials network in Southeast Asia to conduct research on emerging infectious diseases, with an initial emphasis on influenza.

Influenza is by no means the only emerging and re-emerging infectious disease threat that the world faces. For example, malaria is a substantial and growing problem compounded by the emergence of drug-resistant malaria parasites and insecticide-resistant mosquito vectors. NIAID supports a large malaria research portfolio; one recent study identified a specific parasite gene that is essential for full maturation of the parasites in mice. Disrupting this gene not only prevented the onset of disease in mice, but injection of the modified parasites stimulated an immune response that protected them from subsequent infection with unmodified, fully-virulent malaria parasites. This indicated that genetically attenuated parasites might be useful as a malaria vaccine in the future.

Tuberculosis (TB) is an example of a microbial disease that has reemerged in recent years. Infection with *Mycobacterium tuberculosis* is estimated to be prevalent in one-third of the world's population and is especially common among persons infected with HIV. NIAID supports a large portfolio of research to develop new drugs, vaccines, and diagnostics for TB and to evaluate improved treatment and preventive regimens. Recently, two novel, engineered TB vaccines developed with NIAID support entered Phase I clinical trials in the United States. These promising candidates are the first new TB vaccines to be tested in people in more than 60 years. In addition, the Global Alliance for TB Drug Development and NIAID have collaborated to develop a promising new TB drug candidate, which is now being tested in clinical trials. NIAID also has made substantial research progress on West Nile Virus, multi-drug resistant tuberculosis (MDR-TB), SARS, and other new or re-emerging infections.

HIV/AIDS RESEARCH

HIV/AIDS was first recognized as an emerging disease only 25 years ago. Today it is a global catastrophe. According to the Joint United Nations Program on HIV/AIDS (UNAIDS), approximately 40 million people worldwide are living with HIV/AIDS, and their number is increasing by more than 5 million people every year—about 14,000 each day. In the United States, more than one million people are living with HIV/AIDS, and approximately 40,000 new infections occur annually. Worldwide, more than 25 million people with HIV have died since the pandemic began, including more than 520,000 in the United States. In 2004, there were 3 million deaths worldwide due to HIV/AIDS. These statistics are grim reminders of the physical and emotional devastation to individuals, families, and communities coping with HIV/AIDS, and of the terrible impact of HIV/AIDS on regional and global security and the global economy.

Development of a vaccine that protects against HIV/AIDS is one of the highest priorities of the NIAID. The scientific challenges that must be overcome, however, are extraordinary. Because the immune system, with rare exceptions, has not been shown to contain HIV on its own, an HIV vaccine will have to elicit an even stronger immune response than elicited by natural HIV infection if it is to prevent infection. To help meet these challenges, NIAID established the Center for HIV/AIDS Vaccine Immunology (CHAVI) in June 2005. CHAVI's mission is to tackle the fundamental immunological obstacles in HIV vaccine research and to design, develop, and test novel HIV vaccine candidates. The establishment of CHAVI complements NIAID's continued support of other innovative research projects conducted through a highly cooperative and collaborative global research and development program.

Among many HIV vaccine research efforts, NIAID scientists have developed a two-part vaccination strategy, consisting of an initial (prime) vaccination followed by a later (boost) vaccination. The priming dose is a "naked" DNA vaccine, and the boost is a recombinant adenovirus vaccine, which is based on a highly attenuated

version of a common cold virus. Both components contain genes from three different subtypes of HIV that together cause about 85 percent of all HIV infections around the world. An initial Phase I clinical trial showed that the pair of vaccines was well-tolerated and induced substantial immune responses. Building on these promising findings, NIAID recently launched a second phase of testing of this “prime-boost” strategy. This project is a collaboration between three international clinical trial networks—NIAID’s HIV Vaccine Trials Network, the non-profit International AIDS Vaccine Initiative, and the U.S. Military HIV Research Program—and expands the safety and immunogenicity testing of the prime-boost strategy in the Americas, South Africa, and Eastern Africa. Also underway and slated to complete enrollment this year is the evaluation of a candidate adenoviral vaccine administered without a DNA vaccine to determine whether it may be useful alone in preventing HIV infection or disease.

The use of potent combinations of anti-HIV drugs, many of which were developed with NIAID support, has dramatically reduced the numbers of AIDS deaths in industrialized countries. Most recently these drugs have had a major impact on several developing countries in sub-Saharan Africa, the Caribbean, South America and Asia, as drugs have become available to them. Indeed, these drug regimens have transformed the complexion of HIV/AIDS throughout the world, saving the lives of millions of people. These results are some of the most cogent examples of the practical benefits of NIH-supported research. But we cannot be complacent in our success. Anti-HIV drug regimens often cause serious side effects and frequently lose their effectiveness due to the emergence of resistant forms of HIV within a patient. Clinical research is moving new classes of AIDS drugs closer to market and defining how to optimally use currently licensed medications. Basic HIV research continues to uncover additional viral and cellular targets for therapy. For example, several potential drug targets have been identified by determining the mechanisms that HIV uses to gain entry into host cells. These include fusion inhibitors, the first of which was recently approved by the Food and Drug Administration (FDA). In addition, several inhibitors of the HIV enzyme that allows the virus to enter and integrate into an infected cell’s genes have shown great promise in clinical trials.

BIODEFENSE RESEARCH

The potential use of biological agents in a terrorist attack is a serious threat to the citizens of our nation and the world. Research to mitigate this threat is a key focus of NIAID. The NIAID Strategic Plan for Biodefense Research, developed shortly after the terrorist attacks of 2001, outlines three essential pillars of the NIAID biodefense research program: infrastructure needed to safely conduct research on dangerous pathogens; basic research on microbes and host immune defenses that serves as the foundation for applied research; and targeted, milestone-driven development of medical countermeasures to create the vaccines, therapeutics and diagnostics that we would need in the event of a bioterror attack. Implementation of this plan enhances not only our preparedness for bioterrorism, but also for naturally occurring endemic and emerging infectious diseases. In addition, NIAID was recently given the role of coordinating and facilitating NIH research into countermeasures to mitigate harm to civilians from chemical and radiological/nuclear weapons. Other NIH Institutes and Centers will also contribute substantially to these efforts. The NIH Strategic Plan and Research Agenda for Medical Countermeasures against Radiological and Nuclear Threats was released in June 2005, and the NIH Strategic Plan and Research Agenda for Medical Countermeasures against Chemical Threats is scheduled to be released in mid-2006.

Perhaps the most tangible signs of NIAID’s biodefense research progress are the biocontainment research facilities now under construction, which will be capable of safely containing dangerous pathogens, enabling scientists to study such agents. For example, through its extramural program, NIAID is supporting the construction of two National Biocontainment Laboratories—capable of safely containing the most deadly pathogens—as well as thirteen Regional Biocontainment Laboratories nationwide. In addition, three intramural biocontainment labs—on the NIH campus, on the National Interagency Biodefense Campus at Fort Detrick in Frederick, MD, and at the NIAID Rocky Mountain Laboratories in Hamilton, MT—are either complete or under construction. NIAID also has established a nationwide network of Regional Centers of Excellence (RCEs) for Biodefense and Emerging Infectious Diseases Research; two new RCE awards were announced on June 1, 2005, bringing the total number of RCEs nationwide to ten.

The investment in biodefense research has already yielded substantial dividends, some of which are of immediate benefit while others provide considerable promise for the future. Our basic research and clinical trials have already greatly increased

our ability to respond to the threats of smallpox, anthrax, and Ebola with new and improved vaccines. For example, in November 2004, DHHS awarded a contract for the acquisition of 75 million doses of a new anthrax vaccine to be held in the Strategic National Stockpile. NIAID's support of the development of this vaccine was instrumental in making this initiative possible. In addition, NIAID-supported scientists recently discovered that a poxvirus infection may be halted by a cancer drug aimed not at the virus, but at the host cellular machinery that the virus needs to spread from cell to cell. Although much work remains, this research provides a lead to not only a new therapeutic approach to poxviruses such as smallpox, but also a means of circumventing antiviral drug resistance for other viruses. In another example of critical new discoveries, NIAID-supported scientists demonstrated that host cell proteins called cathepsins play an essential role in the Ebola virus' ability to enter and infect cells, and that inhibitors of cathepsin activity block viral entry and reduce the production of infectious Ebola viruses. This suggests that drugs that inhibit the activity of cathepsins might be useful as anti-Ebola therapies.

NIAID's implementation of its Strategic Plan for Biodefense Research has been aided by the enactment of the Project BioShield Act of 2004. Project BioShield provides NIH additional flexibility in awarding contracts, cooperative agreements, and grants for research and development of critical medical countermeasures. The BioShield Act also provides NIH with streamlined personnel authority, which has allowed NIAID to hire highly-qualified individuals to fill key positions related to product development. Lastly, Project BioShield provides NIAID with additional authority for the construction of research facilities, which NIAID used to award grants in fiscal year 2005 for the construction of four Regional Biocontainment Laboratories.

RESEARCH ON IMMUNE-MEDIATED DISEASES

Autoimmune diseases, allergic diseases, asthma and other immunologic diseases are significant causes of chronic disease and disability in the United States and throughout the world. Autoimmune diseases affect 5 to 8 percent of the U.S. population; asthma and allergic diseases together are the sixth leading cause of chronic disease and disability in this country; and asthma is the leading cause of hospitalizations and school absences among children. A promising strategy to treat and prevent immune-mediated diseases is known as immune tolerance. Immune tolerance therapies are designed to preprogram immune cells in a highly specific fashion to eliminate injurious immune responses, such as those seen in autoimmune diseases, while preserving protective responses needed to fight infection. The NIAID has established a comprehensive program in immune tolerance research, including basic research, preclinical testing of promising strategies in nonhuman primates, and clinical evaluation through the Immune Tolerance Network (ITN), a consortium of more than 80 investigators in the United States, Canada, Western Europe, and Australia. Currently, NIAID is supporting more than 40 clinical trials of immune tolerance strategies to treat autoimmune diseases, allergic diseases, and transplant rejection.

NIAID-supported research in immune-mediated diseases has led to significant advances in our understanding of how to manage these diseases. For example, NIAID-supported researchers recently identified novel ways to non-invasively assess the risk of kidney graft rejection by using immunologic and genetic biomarkers present in urine. If validated in larger studies, these biomarkers would allow physicians a non-invasive way to monitor transplant recipients for organ rejection, and intervene before organ injury, a significant advance in the clinical management of transplant patients.

NIAID also remains committed to improving the health of children with asthma, particularly those who live in our Nation's inner cities. For example, NIAID-supported researchers recently published the results of a study on the effect of home-based interventions that reduce exposure to common allergens such as cockroaches, house dust mites, and tobacco smoke. The study found that the interventions resulted in 20 percent fewer days with asthma symptoms and 14 percent fewer unscheduled clinic visits through the intervention year. We anticipate that our extensive research portfolio will continue to illuminate the causes of asthma and other immune-mediated conditions, and lead to new interventions to reduce the burden of these serious diseases.

CONCLUSION

The research conducted at NIAID and at NIAID-sponsored laboratories encompasses a broad array of basic, applied and clinical studies. This research has resulted in tangible benefits to the American public and to individuals throughout the world. By supporting talented researchers and emphasizing a balance of basic stud-

ies and targeted research, we hope to continue to develop innovative technologies and treatments to combat a wide range of important diseases that afflict humanity.

PREPARED STATEMENT OF DR. ELIZABETH G. NABEL

Mr. Chairman and Members of the Committee: I am pleased to present the fiscal year 2007 President's Budget request for the National Heart, Lung, and Blood Institute (NHLBI). The fiscal year 2007 budget includes \$2,901,012,000, a decrease of \$20,745,000 over the fiscal year 2006 enacted level of \$2,921,757,000.

The NHLBI was established as the National Heart Institute in 1948 with a mandate "to improve the health of the people of the United States" through research on diseases of the heart and circulation. And that is exactly what we have done. I believe it is no exaggeration to claim that, over the past decades, biomedical research has made more progress in cardiovascular disease than in any other major chronic health problem. The impact on death rates alone constitutes a monumental validation of this country's public investment in the NIH and the NHLBI.

The United States experienced an epidemic of coronary heart disease (CHD) during the twentieth century and, had the trend continued unabated, more than 1.6 million lives would be lost to CHD this year. In actuality, the toll will be less than 500,000 deaths, reflecting a 63 percent decline in age-adjusted mortality since 1950.¹ Mortality from stroke, the third most common cause of death in the United States, declined 70 percent over that time. The effect on longevity has been remarkable—looking just at recent data, we can see that between 1970 and 2000 the life expectancy of the average American increased by 6 years, and nearly 4 years of that gain was due to reductions in deaths from cardiovascular disease.

Much of the reduction in death rates has come from improved treatments for CHD. Not so long ago, atherosclerosis followed an inexorable course and, once an artery became occluded, blood flow could not be restored. Increasingly sophisticated technological developments in revascularization—coronary artery bypass surgery (1968), balloon angioplasty (1977), stents (1994), and now "drug-eluting" stents—coupled with vastly improved diagnostic procedures and new medications, have literally given many patients a new lease on life. NHLBI-supported basic and applied research studies, as well as carefully designed clinical trials, have enabled scientists to develop these interventions, to assess their utility and safety, and to determine the characteristics of patients most likely to benefit from them. Millions of Americans suffer from cardiovascular disease, and this research has contributed enormously to our ability to help them live longer and healthier lives.

We are equally pleased to reflect on improvements that have occurred in our ability to treat acute heart attacks. In past generations, doctors could only stand by while a heart attack ran its course and they had little to offer the patient but bed rest and a prognosis of rapid death or severely restricted life as a "cardiac cripple." All that changed in the 1980s when scientists determined that most heart attacks occur because of a blood clot in an artery that feeds the heart. The development of thrombolytic—"clot-busting"—therapy followed. NHLBI-sponsored clinical trials of thrombolysis demonstrated that the procedure could limit the area of damaged heart muscle and decrease mortality. This was revolutionary, and it rapidly influenced how heart attack is treated.

The greatest benefit of thrombolysis, however, accrues in the initial minutes and hours after onset of the attack and, unfortunately, many patients do not reach the emergency room in time. In the 1990s the NHLBI initiated a successful trial of community-based interventions to reduce delays in seeking and receiving treatment for heart attack symptoms. The knowledge gained was used to develop Act in Time to Heart Attack Signs, a far-reaching public education campaign launched by the NHLBI during the NIH budget doubling. Also during the doubling, the Institute began a pilot program at Suburban Hospital to test a new approach to diagnosing heart attack patients who may be candidates for thrombolytic therapy. For many patients arriving at the emergency room with chest pain, diagnosis requires measurement of enzymes that appear in the bloodstream only hours after the heart attack has occurred—too late for effective thrombolysis. The experimental program is having great success in using MRI (magnetic resonance imaging) technology to provide a diagnosis in about 35 minutes, and we believe it may form the basis for a better approach to delivering prompt therapy to patients who are likely to benefit from it. In light of recent evidence that thrombolytic therapy may benefit patients who experience a clot-based stroke, we have also teamed up with the National Insti-

¹Data in this statement regarding mortality and life expectancy are from U.S. Vital Statistics.

tute of Neurological Disorders and Stroke to use MRI in evaluating patients who come to the emergency room with stroke symptoms.

Let me mention some special efforts to improve treatment of coronary heart disease in a highly vulnerable population—patients with obesity and type II diabetes. Although there is near-universal optimism that a cure for diabetes will ultimately be found, in the meantime the majority of patients are suffering and dying from cardiovascular disease. We are working to identify approaches to prevent and treat these complications, and I am happy to note that the budget doubling enabled us to move forward with full funding of two major new clinical trials in this area. The ACCORD trial is testing the extent to which control of blood pressure, cholesterol, and glucose levels to thresholds beyond those that are currently recommended will reduce the occurrence of cardiovascular problems. The BARI-2D trial, focused on diabetic patients who already have coronary heart disease, is weighing the merits of revascularization versus medical treatment and, in addition, studying two different approaches to controlling blood sugar. These trials are effortful and expensive because they involve multiple complex issues in diabetes management. However, they address a critical public health need, given the escalating prevalence of obesity and diabetes in the United States, and many among us are likely to benefit from their findings.

Much as we celebrate these advances in treatment, let me assure you that we have never lost sight of our ultimate objective—prevention. Indeed, we have had considerable success in identifying risk factors such as high blood pressure and cholesterol, developing and evaluating methods to control them, and translating the research findings into messages for health-care professionals, patients, and the general public. During the budget doubling, we launched The Heart Truth, an education campaign to raise awareness that heart disease is the leading cause of death in American women and call women to take action to reduce their risk of developing heart disease. Already we have evidence that the campaign's message, "Heart disease doesn't care what you wear—it's the #1 killer of women," has raised awareness throughout the nation. Last June we launched We Can! (Ways to Enhance Children's Activity and Nutrition), a national education program to help children 8–13 years of age stay at a healthy weight. We Can! offers parents and families tips and activities to encourage healthy eating, increase physical activity, and reduce sedentary or screen time. It also provides resources to help community groups and health professionals work toward these goals.

Much of what we know about factors that put people at risk of developing cardiovascular diseases has come from the multigenerational Framingham Heart Study, begun in 1948. I am delighted to announce that the NHLBI, in conjunction with Boston University, recently unveiled a plan to take this study to the next level. Our new Framingham Genetic Research Study will entail up to 500,000 analyses of the DNA of 9,000 study participants. By identifying genetic variations that relate strongly to participant characteristics (e.g., blood pressure and cholesterol levels, overweight and obesity) and to outcomes (e.g., stroke, congestive heart failure, diabetes), we hope to refine our understanding of individual risk and identify carefully focused new strategies for treatment and prevention. We at the NHLBI share Dr. Zerhouni's vision of an approach to medical care that is predictive, personalized, and preemptive and we believe this new endeavor constitutes a major step toward realizing that goal.

PEDIATRIC HEART AND LUNG DISORDERS

Tremendous progress has been made in treating congenital cardiovascular malformations, the most common type of birth defect in the United States. Many of us remember when these conditions constituted a death sentence, but today we have an array of surgical and medical treatments, as well as reliable and effective methods for providing monitoring and support. As a result, more than 90 percent of these babies live to celebrate a first birthday. Indeed, the prognosis has improved so much that there are now more adults than children living with congenital heart defects, according to data from the Adult Congenital Heart Association. Nonetheless, congenital heart disease is still a major contributor to infant mortality and many challenges remain. Thanks to the budget doubling, we have been able to expand significantly our efforts in this area by funding two additional Specialized Centers of Research in Pediatric Cardiovascular Disease, establishing a clinical research network to enable rapid evaluation of new treatment approaches, and soliciting research proposals to develop devices for infants and children who experience cardiopulmonary failure and circulatory collapse.

As recently as 35 years ago, many premature infants died within hours of birth from neonatal respiratory distress syndrome (RDS), a condition caused by lack of

a substance called surfactant that keeps the lung's air sacs open for breathing. The NHLBI's long-term investment in basic, applied, and clinical research has nearly relegated neonatal RDS to history. With development of special ventilation techniques to sustain babies until their lungs matured, introduction of a prenatal test for lung maturity, and demonstration that antenatal corticosteroid treatment could accelerate lung maturation, U.S. deaths from this disorder fell 60 percent between 1970 and 1984—from 10,000 to 4,000 per year. Then, in the 1980s, NHLBI-supported studies of surfactant structure, function, and regulation and efforts to identify the genes for surfactant proteins culminated in development of surfactant replacement products for testing in clinical trials. Since 1990, when two surfactant treatments were approved for widespread clinical use, neonatal RDS mortality has fallen more than 75 percent, to about 1,000 deaths per year.

ASTHMA

For centuries, asthma was viewed a bronchial spasm problem and treated—with limited success—as such. Our intensive research effort in recent years led to the realization that asthma is a manifestation of chronic inflammation and immune dysfunction. This insight revolutionized treatment, the mainstay of which now is anti-inflammatory medications to treat the underlying disease, with bronchodilators used chiefly for quick relief of symptoms. The NHLBI has also been a pioneer in development of self-management strategies and their application, especially for inner-city minority children; evidence indicates favorable effects on emergency room visits and school absences in this vulnerable population. Results of all these efforts are rapidly incorporated into national guidelines that set the standard for modern asthma management. Clinical research networks have proven invaluable for rapidly assessing new treatment strategies, and during the budget doubling we were able to renew our highly productive adult Asthma Clinical Research Network and initiate the Childhood Asthma Research and Education Network, which addresses pediatric asthma. We also began a program focused on severe asthma. These efforts are enabling us to make good on our promise to patients, “Your asthma can be controlled—expect nothing less.” And we are now talking with increasing confidence about curing asthma, going beyond the initial promise of asthma control.

SICKLE CELL DISEASE

As recently as 1970, the average patient with sickle cell disease died in childhood. Today, life expectancy is about 45 years. NHLBI research has led to a standard of care that begins with screening of newborns, provides prophylaxis for potentially lethal childhood infections, and offers transfusion therapy to prevent stroke in high-risk children. A clinical trial demonstrated the value of the drug hydroxyurea in preventing painful crises, acute chest syndrome (a life-threatening respiratory complication), and need for transfusions in adult patients. With the budget doubling, we have been able to undertake a hydroxyurea trial in children, and also to assess the value of stem cell transplantation as a possible cure. Our hope and expectation is that further gains in longevity and quality of life will be achieved.

I would be pleased to respond to any questions that the Committee may have.

PREPARED STATEMENT OF DR. DUANE ALEXANDER, DIRECTOR, NATIONAL INSTITUTE OF CHILD HEALTH AND HUMAN DEVELOPMENT

Mr. Chairman and Members of the Committee: I am pleased to present the fiscal year 2007 President's budget request for the National Institute of Child Health and Human Development (NICHD). The fiscal year 2007 budget includes \$1,257,418,000, a decrease of \$7,351,000 over the fiscal year 2006 enacted level of \$1,264,769,000 comparable for transfers proposed in the President's request.

The mission of the NICHD is vital to the NIH goal of ensuring the overall health and well-being of the American people. Our research focuses on both child health and human development. Increasingly, researchers are confirming that lifelong health and well-being are strongly influenced by events occurring early in life.

Understanding human development evolves from understanding normal growth and change processes before birth through adulthood. It begins at the most basic molecular and cellular levels and encompasses cognitive, behavioral, physical and social development. By understanding what goes “right,” NICHD research provides clues as to what may go “wrong,” laying the critical scientific foundation not only for understanding many disease processes, but also for preventing them altogether.

FETAL DEVELOPMENT: JUMP START ON LIFE

We now know that both undernourished and obese mothers have children with increased risk of chronic disease later in life. This is a problem world wide and it is an increasing problem in the United States.

To understand and reverse the epidemic of type 2 diabetes among young people, we need to look beyond their diet. The health and nutrition of the mother during fetal development influences not only how children function but also the later development of diabetes, high blood pressure, heart disease and other conditions. To better understand fetal origins of adult disease, researchers recently discovered links between birth weight and stress hormone (cortisol) levels in boys and girls who were small at birth, but healthy term babies. Cortisol helps to regulate blood pressure, energy production, and response to stress. The researchers found that the lower birth weight boys had higher levels of cortisol under stressful conditions compared to the higher birth weight boys. They found that the lower birth weight girls had higher cortisol levels at the beginning of the day. This discovery demonstrates how low birth weight can have lasting, yet different, effects on stress hormone levels in girls and boys. These alterations in cortisol may predispose children to obesity, hypertension, and glucose intolerance later in life.

PREDICTING PREECLAMPSIA

Preeclampsia is a sudden, dangerously high increase in high blood pressure that threatens the health of a pregnant woman and her fetus. Preeclampsia strikes without warning and can result in maternal seizures and even death. The researchers studying this condition found that women who, in mid-pregnancy, have a lower level of a substance known as placental growth factor were more likely to develop preeclampsia. This advance may lead to a screening test for preeclampsia and a treatment to help women avoid the condition.

OBSTETRIC PHARMACOLOGY—TREATMENT FOR PREGNANT WOMEN

Most drugs used to treat pregnant women are prescribed without full knowledge about safety and efficacy. In many cases, no data exists to predict how the drug's dynamics may interfere with a woman's pregnancy. To fill this knowledge gap, the NICHD has established the Obstetric-Fetal Pharmacology Research Units (OFPRU) Network to develop improved safety and efficacy drug information for pregnant women. One drug currently being studied is used to control gestational diabetes. Gestational diabetes affects up to 15 percent of all pregnancies according to the March of Dimes. The condition results from a sudden inability of the body to remove sugar from the blood. Untreated, gestational diabetes results in large, stocky babies who may cease breathing unexpectedly, have difficulty feeding, and must eat frequently to avoid seizures. Children of mothers with gestational diabetes are also likely to become obese during childhood and adulthood.

For many years, physicians treated gestational diabetes with injections of insulin. Recently, however, physicians began treating pregnant women with glyburide, which stimulates the pancreas to gradually release small quantities of insulin. Many patients preferred the convenience of taking a pill to giving themselves an injection. Although many pregnant women have taken glyburide, no studies have ever tested the drug's effectiveness in treating gestational diabetes. A new study is examining the use of glyburide in pregnancy, to determine if the current dosing schedule is the most effective means to treat the disorder.

PREMATURE BIRTH RESEARCH

Reducing preterm birth (PTB) is a major public health priority and a major research priority for this Institute. One out of eight infants in the United States is born preterm. This amounts to about 476,000 infants a year. The March of Dimes estimates that babies born too soon or too small cost the U.S. health system \$18.1 billion a year. Preterm infants face a number of serious health problems and life-threatening conditions. PTB accounts for nearly half of the neurological problems among newborns who are at risk of having learning disabilities and mental retardation. When preterm infants reach adulthood, they also face much higher risks of cardiovascular disease and diabetes.

The NIH investment in preterm birth research is paying dividends. For the first time, we now have a method to reduce the risk of PTB for some women. One of our studies found that weekly injections of a synthetic form of progesterone reduces the chances of preterm delivery in women who had already given birth prematurely. For the first time, this research gives doctors an intervention that has been shown to be both safe and effective in reducing the risks of preterm birth. This discovery also

illustrates how quickly research can be turned into practice. Shortly after this research was published, The American College of Obstetricians and Gynecologists recommended that all of their members use progesterone to prevent PTB for women with previous PTB. Another study found that pregnant women who have a condition known as bacterial vaginosis have a greater likelihood of delivering prematurely. For many years, these women have been treated with antibiotics. Contrary to existing clinical thinking, treating the infection with an antibiotic during pregnancy did not reduce the incidence of preterm birth. Still another NICHD study found that women with a condition known as trichomoniasis are also at increased risk for preterm delivery. The study found that giving antibiotics does not reduce the risk of preterm birth associated with infection; moreover, this treatment actually increased the preterm birth rate.

The new knowledge gained from each of these three studies was created by one of the multidisciplinary clinical research networks supported by the NICHD. With these networks in place, NICHD scientists working with researchers around the country can answer important scientific questions quickly, and work through professional organizations to help clinicians translate the new knowledge into practice.

The NICHD recently established the Genomics and Proteomics Network for Premature Birth Research. This new network will focus on the hereditary information in DNA and the structure and function of proteins to understand the underlying processes that lead to preterm birth.

GENES MAY HOLD THE KEY TO TREATING UTERINE FIBROIDS

Each year, more than 200,000 women in the United States undergo a hysterectomy to treat the chronic pain and abnormal bleeding caused by fibroids. Scientists are exploring alternative ways to treat fibroids without surgery. Previously, these researchers identified a molecule called transforming growth factor beta (TGF- β) that helps to regulate several processes including the growth of uterine fibroids. Using a powerful new technology, the researchers identified the different genes influenced by the growth factor in both normal and fibroid cells. The researchers then tested a gene therapy that appeared to block production and action of TGF- β . This insight may lead to novel, non-surgical therapeutic approaches, not only to prevent uterine fibroid growth, but also to treat other reproductive conditions.

BUFFERGEL SHOWN TO BE SAFE CONTRACEPTIVE

Researchers have made a major step forward in developing contraceptives that protect women against HIV. One product, BufferGel, can be used with a diaphragm, much like a conventional spermicide. The results of a recent study demonstrate that BufferGel is as effective at preventing pregnancy as is currently available spermicides. A study is now in progress to determine if BufferGel can reduce transmission of the AIDS virus.

GENE PROGRAMS EARLY DEVELOPMENT AND NEURAL MIGRATION

NICHD researchers made a significant advance in understanding dyslexia. In an article that Science Magazine called one of the 10 major breakthroughs in 2005, the researchers linked the developmental gene DCDC2 to dyslexia. This gene functions to control nerve cell migration in early brain development. This work suggests that genetic miscues alter brain biology in the womb in a way that predisposes people to problems later in life.

FUTURE RESEARCH: NEWBORN SCREENING

The NICHD Newborn Screening Initiative is moving forward in its effort to develop and employ the latest technology for improving the availability, accessibility, and quality of genetic and other diagnostic laboratory testing for rare diseases and conditions affecting newborns. Ultimately, this research could help identify at-risk infants as early as possible and provide the data needed to develop therapies for many of these conditions. As a cornerstone activity, the NICHD funded a major grant for developing and refining a newborn screening test for spinal muscular atrophy (SMA), a common fatal neuromuscular disease in children. The NICHD will soon be funding additional grants to increase understanding of conditions such as SMA or other genetic conditions.

MATHEMATICS AND SCIENCE COGNITION AND LEARNING

The NICHD is enhancing its program to better understand the underlying developmental processes that allow children to learn math and science. One goal is to

help researchers understand the developmental and cognitive processes needed to help children transition successfully from arithmetic to algebraic reasoning, a fundamental skill needed to allow children to advance their understanding of mathematical concepts. In turn, mastering math-related concepts such as recognizing patterns, representing relationships, and making generalizations is key to learning and understanding science. These critical program activities fill a major research need to clarify the cognitive factors needed for scientific thinking and learning.

COMMUNITY-BASED REHABILITATION INTERVENTION

The aging of the baby-boom generation and expected pressures on the U.S. health care system make research into effective therapies in community settings a high priority. Clinical trials of rehabilitation therapies have demonstrated the efficacy of novel interventions in preventing or significantly lessening disabling conditions associated with stroke, traumatic brain injury, and other disorders and conditions. Little is known, however, about whether and how well such therapies will work in less-controlled community practice settings. Scientists do not know whether—or how—efficacious rehabilitative therapies and even clinical trial design may need to be modified for community settings. To address these critical questions, the NICHD will solicit applications for clinical trials by scientists partnering with persons with disabilities, practitioners, and others in the community.

Mr. Chairman and members of the Committee, the support you have shown for medical research has allowed scientists in research centers around the country to make discoveries that advance the health of women, children and families. I will be pleased to answer any questions.

PREPARED STATEMENT OF DR. BARBARA M. ALVING, ACTING DIRECTOR, NATIONAL CENTER FOR RESEARCH RESOURCES

Mr. Chairman and Members of the Committee: It is a privilege to present to you, for the first time, as the Acting Director of the National Center for Research Resources (NCRR), the President's budget request for NCRR for fiscal year 2007, a sum of \$1,098,242,000, including support for AIDS research, which reflects a net decrease of \$859,000 over the comparable fiscal year 2006 appropriation.

By developing and funding essential research resources, NCRR connects scientists with one another, as well as with patients and communities across the nation. These connections bring together innovative research teams and the power of shared resources, multiplying the opportunities to improve human health.

These connections can be seen in the new institutional Clinical and Translational Science Awards program, launched in fiscal year 2006, which enables researchers to train and collaborate in new ways to move findings in the laboratory more quickly to patients. NCRR also is bringing patients, advocacy groups, and researchers together to fight rare diseases—a unique opportunity to combine patient information and support with research knowledge. Other programs are helping investigators to create technologies that will make research information more accessible and precise through various software tools and Internet connections.

In addition, NCRR-supported technologies help researchers—located in isolated regions—share information that benefits underserved populations across the country. And at NCRR-supported primate research centers, investigators come together to study AIDS vaccines, Parkinson's, Alzheimer's, and many other diseases. Perhaps our most wide-ranging connections are made through science education—programs that reach young and old—on a diverse range of health-related issues.

These are just a few of the programs that comprise NCRR's portfolio, but they illustrate how we are investing research dollars in order to bring the power of shared resources to communities and researchers across the nation and ultimately improve the health of Americans. I would now like to provide you with additional details about each of these exciting programs.

INTEGRATING CLINICAL AND TRANSLATIONAL SCIENCE

Recognizing that a well-integrated collaborative effort is needed to transform basic discoveries into improved medical care, NCRR has launched an important new initiative—the Clinical and Translational Science Awards (CTSAs)—on behalf of the NIH Roadmap for Medical Research. The CTSA Program was initiated to break existing barriers between basic and clinical sciences and, above all, to get people to work together to speed the delivery of improved health care to the public. Developed with extensive input from the scientific community, the CTSAs will help research institutions nationwide create an academic home for clinical and translational re-

search, essentially generating what NIH Director Dr. Elias Zerhouni calls the “glue” that fills the gaps among scientists in multiple disciplines and thus forms a bridge between basic and clinical research.

In ongoing dialogues with the scientific community, researchers also have told us that the CTSA initiative will allow them to strengthen the career development pipeline for clinical and translational researchers. At the same time, it will build partnerships with communities that will ensure that diverse populations, and clinical practitioners serving those populations, play an integral part in addressing the unique health challenges that they face. With the community’s participation, the CTSAs will help to deliver improved medical care that meets the needs of these diverse patients and their communities.

CREATING PARTNERSHIPS: RARE DISEASES NETWORK

Another NCRR initiative—the Rare Diseases Clinical Research Network—illustrates the importance of bringing patients and researchers together. Headed by NCRR in partnership with the NIH Office of Rare Diseases, the network is truly a trans-NIH activity, with funding coming from five additional NIH institutes. The need for such a network is best appreciated when one considers the emotional toll a family faces when they find out that their child has a rare disease and the desperation they face when they search for medical resources. For example, Trish Hertzog, a mother from Philadelphia who agreed that we could tell her story to help others, can vividly recall the day her son Mathew was born more than a decade ago. Unbeknownst to anyone, including his doctors, this seemingly healthy newborn lacked a critical gene that helps to remove toxic substances from the body. Within two days of his birth, Mathew fell into a coma, as lethal levels of ammonia built up in his brain, and died within hours.

Mathew Hertzog had inherited a rare condition known as a urea cycle disorder, which affects only about 1 in 30,000 children. Collectively, rare diseases affect about 25 million Americans, according to the National Organization for Rare Diseases. Research on rare diseases is especially challenging since few patients with the same condition can be recruited from any one clinical site.

To improve outcomes and outreach, the Rare Diseases Clinical Research Network unites the efforts of researchers from multiple institutions and their patients nationwide. The Network’s web site has become a source of information for the public, physicians, patients, and investigators about rare diseases. The site also contains a unique web-based contact registry for patients who wish to learn about clinical studies. With this Network now available, parents like Trish can obtain information about rare diseases and learn about participating in one of the initial clinical trials.

WIDENING THE NET: UNDER-REPRESENTED POPULATIONS AND AREAS

NCRR is using the latest advances in technology to promote greater inclusion of under-represented minority and rural populations in research by boosting capacity in institutions and regions of the country that lack high-capacity, broad-bandwidth Internet connections. Some states—including Montana, Wyoming, Alaska, Idaho, Nevada, and Hawaii—lack access to advanced Internet applications, such as virtual laboratories, digital libraries, distance education, as well as advanced networking capabilities. This lack of resources hinders the ability of the institutions in these states to conduct collaborative, data-intensive biomedical studies. In the first phase of a national effort called IDeANet, NCRR is enhancing high-speed network connectivity in these five rural Western states and Hawaii, which will bring these areas on par with connectivity in the other parts of the country.

This effort is part of the Institutional Development Award (IDeA) Program, which broadens the geographical distribution of NIH funding for biomedical research. Ultimately, IDeANet will expand to include NCRR’s Research Centers in Minority Institutions Program, which enhances the research capacity and infrastructure at minority colleges and universities that offer doctorates in health sciences.

SPURRING ADVANCES THROUGH DATA SHARING

Through the Biomedical Informatics Research Network (BIRN), NCRR supports the integration of data, expertise, and unique technologies to spur scientific advances that would be difficult or impossible in the context of individual laboratories. To illustrate this point, five volunteer research participants traveled across the country to nine different sites to have their brains imaged via magnetic resonance imaging (MRI). The data that was collected contributed to a first-of-its-kind neuroimaging dataset that will enhance large-scale, multisite imaging studies for years to come. Scientists found that brain images from a single individual appeared surprisingly different when collected at different MRI centers—such variance would

greatly hamper multi-site imaging studies. Through BIRN, scientists have recently developed software tools to standardize data and reduce this type of inter-site variability in brain scans. This collaboration is just one example of how BIRN contributes to solving complex health-related problems. While initial efforts are focusing on neuroimaging data, the tools and technologies developed by BIRN ultimately may be applied to other disciplines.

PROVIDING CRITICAL LINKS: NONHUMAN PRIMATE RESEARCH

Studies of nonhuman primates are indispensable to translational research, providing a critical link between small laboratory animals and human subjects. Many of today's life-saving interventions—including polio vaccines, AIDS-fighting drugs, and heart surgery techniques—depended on preliminary evaluation in nonhuman primates like the rhesus macaque. To support such studies, NCRR funds eight highly specialized research facilities known as the National Primate Research Centers, which bring together researchers with a variety of expertise, thereby contributing to studies of major human health issues, including cancer and neurodegenerative disorders.

Because the nation currently lacks a sufficient number of clinically trained primate veterinarians, NCRR plans to support an initiative to attract and train graduate-level veterinarians in the procedures for conducting primate research. A well-trained veterinary research corps will enhance the country's capacity to respond to the emergence and spread of potentially deadly human diseases, such as severe acute respiratory syndrome (SARS), influenza, and hepatitis.

PROMOTING SCIENCE AND HEALTH LITERACY

By supporting collaborations among educators, researchers, community groups, museums, and other organizations, NCRR's Science Education Partnership Award program increases the public's understanding of medical research and delivers information about healthy living and career opportunities in science to children and the general public. For instance, a novel project at the University of Maryland is infusing physical education classes in grades 3–5 with science-enriched curriculum to enhance children's knowledge of the heart and other muscles and the importance of physical fitness. Another project, a partnership involving the University of Hawaii and culturally diverse local communities, is designed to enhance biomedical education and mentoring for children and their teachers on isolated Hawaiian islands. By providing students with opportunities to participate in hands-on, inquiry-based research projects, NCRR hopes to demystify science and make it more accessible to individuals throughout the nation.

CONCLUSION

The future of medical care will depend on our commitment to bring together scientists with diverse expertise and to support research institutions with varying strengths and research capacities. At the same time, we must ensure the participation of researchers and patients who are from ethnically and geographically diverse communities and share the importance of medical research with educators and students. Our goal in the coming year is to enhance these collaborations, partnerships, and networks in order to bring the power of shared resources to researchers across the nation and maximize our research investments.

PREPARED STATEMENT OF DR. JEREMY BERG, DIRECTOR, NATIONAL INSTITUTE OF GENERAL MEDICAL SCIENCES

Mr. Chairman and Members of the Committee: I am pleased to present the fiscal year 2007 President's budget request for the National Institute of General Medical Sciences (NIGMS). The fiscal year 2007 budget includes \$1,923,481,000, a decrease of \$12,137,000 from the fiscal year 2006 enacted level of \$1,935,618,000 comparable for transfers proposed in the President's request.

NIGMS supports a broad spectrum of research central to the National Institutes of Health's mission of improving the nation's health. Over the years, this foundational work has led to important breakthroughs and treatments. Biophysical studies sparked the development of life-saving drugs for AIDS. Inventive burn and trauma research yielded the first artificial skin to treat severely burned patients. Most recently, research in pharmacogenetics led the Food and Drug Administration (FDA) to change the label of irinotecan, a drug approved in 1996 for colorectal, lung, and other cancers. The label now indicates that people with a certain genetic vari-

ation are at a greater risk for life-threatening reactions to the drug and encourages doctors to use a lower starting dose for those patients.

In other areas, such as chemistry, groundbreaking basic research helped support drug development by the pharmaceutical industry. NIGMS' investment in this area was recognized with the 2005 Nobel Prize in chemistry, bringing the number of laureates whose research we have funded to 57. Long-time grantees Robert H. Grubbs, Ph.D., of the California Institute of Technology and Richard R. Schrock, Ph.D., of the Massachusetts Institute of Technology were honored for developing a revolutionary way of synthesizing new molecules. Their discoveries transformed a seemingly esoteric process into a practical tool that is now routinely used in the pharmaceutical industry and in other areas of the economy, including the plastics industry.

STRENGTHENING THE PIPELINE

In addition to providing stable research support to these chemists, NIGMS provided funds to support their transition from trainees to independent researchers. The Institute has a number of structured programs that offer thousands of trainees access to state-of-the-art resources, rigorous curricula, and high-quality ethics training. Each year, many scientists receiving NIGMS support launch independent careers and join the ranks of top-notch researchers in a wide range of scientific disciplines.

Many creative contributions like the few I have highlighted above are the work of individual bright minds. However, as biomedical research converges and scientific fields meld together in new ways, researchers working in different areas need to combine their talent and expertise. Recognizing the dual need for teamwork and individual intellectual contribution, NIGMS has invested its resources wisely. In addition to funding a substantial number of individual investigators, we have broadened our investment by funding large, multidisciplinary scientific teams. These programs have served a truly catalytic role in tackling issues of great importance to public health, and I would like to describe some of their recent advances.

THE DAWN OF PERSONALIZED MEDICINE

The NIGMS-led Pharmacogenetics Research Network (PGRN), a trans-NIH project consisting of 12 scientific teams, has just completed its first 5 years of work with an impressive track record. For example, the treatment of childhood leukemia is improving due to the discovery that variations in two genes can predict which patients with the most common form of the disease have a higher risk of relapse. On the horizon is safer dosing of the widely used blood-thinning medicine Coumadin® (also known as warfarin) due to the discovery that normal variation in two genes can put some patients at risk for excessive bleeding or for heart attacks and strokes. PGRN researchers have also made important strides in unraveling disparities in response to treatments for asthma, a disease that affects roughly 20 million Americans, according to the American Lung Association. Recent findings show that variation in just a few genes affects responses to two mainstay asthma therapies, inhaled steroids and beta-agonists. Genetic tests to detect these variations may be available within a year.

Other payoffs from NIGMS investments in pharmacogenetics extend beyond implications for individual drug dosing. PGRN research has unexpectedly uncovered knowledge that can predict disease risk in subsets of patients, including those taking tamoxifen for breast cancer and beta-blockers for heart disease. Finally, NIGMS-sponsored research in pharmacogenetics is having an impact on policy. PGRN studies have played a role in the FDA's recent decision to develop new guidelines for personalized medicines. For example, an FDA program that allows manufacturers to submit pharmacogenetic data for review has seen a jump from six submissions to 25 in the space of 1 year.

TEAMING SCIENCE FOR PUBLIC HEALTH GAINS

NIGMS' innovative "glue grant" program is a novel approach that brings together scientists from different disciplines to attack problems beyond the scope of an individual investigator but crucial to the future of the public health enterprise. One example of a recent glue grant advance is the discovery that genes can help explain why patients can have dramatically different reactions to traumatic injury. The NIGMS-funded Inflammation and the Host Response to Injury research group, which performed this study, will also release this year a set of standard operating procedures for the care of critically injured patients. This work, while still in the early stages, is moving ahead rapidly and will likely improve standards for treatment across the nation as well as facilitate the conduct of high-quality research in this important field.

Many areas of basic biomedical research require an incubation period before results emerge and new knowledge is translated into the clinic. Both pharmacogenetics and much of the complex biology being investigated with glue grants are good examples, and the recent achievements I've described offer evidence that the wait has been worth it. However, in other circumstances NIGMS has invested basic research expertise in areas quite ripe for practical development. A case in point is the Models of Infectious Disease Agent Study (MIDAS), not yet 2 years old, which has already made an important mark on the public health policy landscape. Several key papers have emerged from this highly interdisciplinary effort, and the program continues to be fluid, evolving to match public health needs. The MIDAS network is focusing on modeling the spread of influenza, and its models are providing key inputs to policy makers and health officials engaged in preparing for possible influenza pandemics.

VALUE OF A SYSTEMS APPROACH

The ready application of MIDAS research to current flu preparedness efforts is apparent, but I'd like to point out that this research is a shining example of what may seem a more esoteric concept: systems biology. In fact, systems biology is a powerful and promising approach for investigating how to control the progression of diseases worldwide.

Systems biology addresses how the parts of a complex network work together to produce the behavior of the overall system. The threads of systems biology are apparent in pharmacogenetics, which goes beyond the consideration of a drug and its target to examine other molecules that affect drug action and determine how apparently subtle variations in these molecules can affect drug efficacy and safety. In infectious disease modeling, the properties of an infectious agent are superimposed on the structure of society, from transportation networks to human behavior. Systems biological approaches require interdisciplinary teams of scientists working together toward a common goal that is often closer to practical applications than are the powerful, "one component at a time" approaches that have driven biomedical research so successfully over the past decades.

POWER OF THE MIND

Let me finish by returning to the contributions of individual minds. I'll highlight two relatively young scientists who have been recognized by the NIH Director's Pioneer Award program for their exceptional potential to make major breakthroughs.

The first is Sunney Xie, Ph.D., of Harvard University. He is a pioneer in the development of methods that can see single biological molecules in action. Most biomedical experiments examine millions or more molecules, revealing the average behavior of all of them. While this information can be highly useful, many details are lost. Dr. Xie's methods, developed through an inspired application of techniques from physics and chemistry, look at the behavior of one molecule at a time. This is like being able to hear one conversation clearly rather than hearing the din of a room full of people all talking at once. As these methods mature, they have the potential to transform our understanding of how gene expression is controlled in normal and diseased cells.

The second NIH Director's Pioneer Award winner I will mention is neurobiologist Erich Jarvis, Ph.D., of Duke University. Dr. Jarvis, an African American who grew up amid poverty, drugs, and violence in Harlem, seeks to unravel the mysteries of vocal learning. He is investigating this question using songbirds as a model system, and he has already made important strides in unlocking some of the complexity of one of biology's unexplored frontiers: the brain. Although his research falls outside the realm of the NIGMS mission and Dr. Jarvis is not currently an Institute grantee, I tell you his story for a different, very important reason. He is a terrific example of what we stand to lose if we do not continue to invest in the creative individual sparks of young scientists in our diverse society. At least part of Dr. Jarvis's rise to success can be attributed to chances he got in school. He participated in the NIGMS Minority Biomedical Research Support and Minority Access to Research Careers programs as an undergraduate at the City University of New York, Hunter College, where he received a bachelor's degree in biology and mathematics. He later earned a Ph.D. in molecular neurobiology and animal behavior from the Rockefeller University and today works at the forefront of an exciting discipline at the intersection of biomedical and behavioral research.

The creative energies of potential biomedical researchers—not just those in fields traditionally related to biomedicine but also those in associated fields in the physical, mathematical, behavioral, and social sciences—will drive advances leading to improvements in human health for many years to come. Nurturing a diverse sci-

entific workforce will enhance the vitality of our nation and improve the health of our children and their children.

Thank you, Mr. Chairman. I would be pleased to answer any questions that the Committee may have.

PREPARED STATEMENT OF DR. PATRICIA A. GRADY, DIRECTOR, NATIONAL INSTITUTE OF NURSING RESEARCH

Mr. Chairman and Members of the Committee: I appreciate the opportunity to present the fiscal year 2007 President's budget request for the National Institute of Nursing Research (NINR). The fiscal year 2007 budget includes \$136,550,000, a decrease of \$792,000 over the fiscal year 2006 enacted level of \$137,342,000 comparable for transfers proposed in the President's request.

I am pleased to describe some of the exciting research of the National Institute of Nursing Research (NINR). NINR is charged with supporting research that establishes the scientific basis of quality patient care regardless of disease or health status. We fund research that affects individuals across the lifespan and all health care settings, especially the underserved.

NINR is currently celebrating the 20th anniversary of its establishment at NIH. We have used this occasion not only to take stock of our accomplishments, but more importantly, to look toward the future role of NINR's research in today's increasingly complex health care environment. We are faced with an aging population at a time when our Nation is experiencing a shortage of nurses. We are also in an era of new technologies, which demands that nurses be technologically-savvy and able to adapt these new methods to a variety of patient populations and settings. This dynamic health care environment provides many opportunities for nursing research to address a variety of challenges and improve health care for all patients.

Let me give you a few examples of how our research has improved lives and the promise it holds for the future.

HEALTHY MOTHERS AND HEALTHY CHILDREN

Sleep and Healthy Pregnancies.—Women often complain of fatigue and difficulty sleeping during pregnancy, especially as they approach delivery. Researchers studied women who slept less than 6 hours per night or who experienced frequent sleep disturbances during their pregnancy. These women had significantly longer labors and were 3–4 times more likely to have a cesarean delivery than women who slept 7–8 hours a night with fewer disruptions. These results highlight the importance of adequate sleep during pregnancy, and suggest a need for care providers to stress better sleeping habits to their pregnant patients.

Children and Health Disparities.—In fiscal year 2007, NINR will solicit new intervention research proposals aimed at reducing health disparities among children. NINR is committed to reducing disparities in health care, but current research in this area often targets adults. Children who live in poverty have little access to health care, and these children are disproportionately from minority populations. NINR's effort to reduce disparities in child health will target such areas as: developing culturally-sensitive interventions to promote physical activity and healthy diets in children, reducing health risk factors in children that lead to poor health outcomes, and studying how gender and immigrant status affect child health and access to health care.

STAYING HEALTHY THROUGHOUT ADULTHOOD

Culturally-sensitive Diet Intervention.—Diabetes is prevalent among rural African-Americans, and compliance with dietary self-management guidelines is often poor. In one study, NINR researchers tested a dietary intervention for diabetic African-Americans living in rural South Carolina. Through culturally-tailored classes that taught healthy food choices and low-fat cooking techniques, participants successfully lowered their body weight and fat intake. Other community-based interventions that include culturally-relevant components show similar successes. These types of programs may be important tools in promoting health and reducing health disparities.

Heart Disease in Women.—Heart disease, the number one cause of death in the United States, is sometimes more difficult to diagnose in women than in men, because women can exhibit different symptoms of heart disease than men. Better ways of detecting heart disease are therefore needed. NINR investigators are currently developing and testing a new screening tool that could predict whether or not certain women are at risk for serious heart disease. The test takes into account the

different symptoms that women with heart disease experience, and it factors in the diverse symptoms experienced by women of different races.

UNDERSTANDING AGING AND CARING FOR THE ELDERLY

Improving Self-management for the Elderly.—The aging American population has tremendous implications for our health care system. Better tools are needed to prevent and treat the health problems experienced by the elderly in a cost-effective manner. Improving self-management strategies is one way to decrease hospital and long-term care costs. Health professionals have developed telehealth programs that allow elderly patients to monitor and manage their symptoms at home by communicating with their providers over the phone or the internet. However, the effectiveness of telehealth interventions has not been well-studied. NINR investigators are currently testing a self-management telehealth intervention for patients with heart failure. The investigators will study questions such as: Is the intervention more effective than traditional methods of treatment? Are elderly patients willing to use the new technology? Do these techniques save money? Findings from these studies may help providers better use technology in self-management. This could ultimately lead to a higher quality of life for patients, and lower health care costs for consumers.

Caregivers and Depression.—An aging population also means that an increasing number of spouses and children will be caring for their infirm partners or parents. In addition to significant economic and societal costs,¹ caregiving may also have serious negative health impacts. Caregiving can often be a stressful and time-consuming experience for those who take on the responsibility. NINR has funded a wide range of studies to analyze the burdens experienced by caregivers and develop methods to alleviate these burdens. One group of NINR researchers surveyed over 2,000 female caregivers of elderly veterans with dementia and found that over one-third of the caregivers exhibited symptoms of depression. However, less than one in five of those with depression were using antidepressants; Caucasians were twice as likely as African-Americans to be taking such medications. These results suggest that caregivers should be routinely screened for depression and that better efforts may be needed to educate informal caregivers about the potential benefits of antidepressant therapy.

PATIENTS AND FAMILIES AT THE END OF LIFE

The final stage of life is a challenging time for everyone involved, from the patient, to attending physicians and nurses, and to bereaved family and friends. NINR is the lead NIH institute for end-of-life research. We are charged with finding ways to improve end-of-life care for all involved and ensure that patients experience death with as much dignity and comfort as possible. We fund research on such topics as: better management of symptoms prior to death; improving communication between doctors, patients, and family members; and examining factors that influence end-of-life decision-making. NINR researchers continue to make important findings in these areas.

Communicating with Families at the End of Life.—One study found that physicians in intensive care units often fail in communicating with family members when discussing the withholding or withdrawal of care from a dying patient. Problems included failures to listen to the concerns or address the emotions of the family members. Physicians also failed to properly explain the uses and purpose of palliative care or the ethical basis for deciding to remove life-prolonging therapies. A better awareness of these gaps can help physicians and nurses improve their communication skills for talking to families in difficult times.

NURSING SHORTAGES AND TRAINING NURSE RESEARCHERS

The current aging of our population comes at a time when the supply of nurses in the United States cannot meet the demand. In addition, new advances in medical technology require a more technologically-savvy nursing workforce. There was a shortage of approximately 168,000 registered nurses in the United States in 2003, and this shortage is expected to top 1 million by 2020. The field of nursing research is experiencing the effects of this shortage. Fewer nurses mean fewer nurse researchers, and that means fewer nursing faculty.

NINR continues to fund innovative initiatives to train new nurse researchers. Our Nursing Partnership Centers to Reduce Health Disparities partner research-inten-

¹Langa KM, Chernew ME, Kabeto MU, Herzog AR, Ofstedal MB, Willis RJ, Wallace RB, Mucha LM, Straus WL, Fendrick AM, National Estimates of the Quantity and Cost of Informal Caregiving for the Elderly with Dementia. *J Gen Intern Med* 16: 770–778, 2001.

sive universities with minority-serving institutions to increase the number of researchers from underserved populations. We also continue to collaborate with universities on training students in fast-track baccalaureate-to-doctoral programs to speed the process of developing new nurse scientists and faculty.

NINR AND THE NIH ROADMAP

NINR has incorporated two key themes of the NIH Roadmap into its research agenda: Interdisciplinary Research Teams of the Future and Re-engineering the Clinical Research Enterprise. Historically, NINR has maintained a focus on interdisciplinary research, but increased collaborations made possible by the Roadmap have fully introduced nursing science to the rest of the scientific community. They have also enabled nurse scientists to expand the breadth of their own work. Because of the strongly clinical emphasis of the NINR research portfolio, the Roadmap's clinical research initiatives are ideally suited to NINR. We will actively pursue Roadmap initiatives that seek to develop new technologies to measure patient symptoms and quality of life, and others that strive to develop skilled clinical investigators with strong multidisciplinary backgrounds.

CONCLUSION

In conclusion, NINR continues to discover effective approaches to meeting the challenges of today's dynamic health care environment, while looking ahead to meet the health care needs of tomorrow. We will strive to improve the quality of care and quality of life for all individuals, especially the underserved, regardless of age or disease. We will also train the next generation of leaders in nursing research. The past twenty years have demonstrated the power of nursing research. The future holds endless opportunities.

Thank you, Mr. Chairman. I will be happy to answer any questions that the Committee might have.

PREPARED STATEMENT OF DR. RICHARD J. HODES, DIRECTOR, NATIONAL INSTITUTE ON AGING

Mr. Chairman and Members of the Committee: The NIA is requesting an fiscal year 2007 budget of \$1,039,828,000, a decrease of \$6,803,000, or .6 percent below the fiscal year 2006 enacted level.

Thank you for this opportunity to participate in today's hearing. I am Dr. Richard Hodes, Director of the National Institute on Aging, and I am pleased to be here today to tell you about our progress making and communicating scientific discoveries that will improve the health and well-being of older Americans.

There are today approximately 35 million Americans ages 65 and over, according to the U.S. Bureau of the Census, and this number is expected to rise dramatically in the coming decades as members of the Baby Boom generation reach retirement age. These older Americans are more likely than at any other time in history to enjoy good health and an active lifestyle: Data from the National Long Term Care Survey (NLTCS) indicate that the rate of disability among older Americans dramatically declined from the 1980s through the mid 1990s, even among the "oldest old," people age 85 and older. At the same time, however, the downward trend in disability among the elderly may be in danger of reversal. Data from the National Health Interview Survey show that, over the same period, the disability rate actually rose significantly for people ages 18-59, with the growing prevalence of obesity an important factor in this trend. Now, in fact, some demographers are forecasting a complete leveling-off of the disability decline in the coming decade.¹

The mission of the National Institute on Aging (NIA) is to improve the health and well-being of older Americans through research. In support of its mission, the Institute conducts and supports an extensive program of research on all aspects of aging, from the basic cellular and molecular changes that occur as we age, to the prevention and treatment of common age-related conditions, to the behavioral and social aspects of growing older, including the demographic and economic implications of an aging society. In addition, the NIA is the lead Federal agency for research related to the all-important effort to prevent and treat Alzheimer's disease (AD). Finally, our education and outreach programs provide vital information to older people

¹Goldman DP et al. Consequences of Health Trends and Medical Innovations for the Future Elderly. Health Affairs online special issue "Health and Spending of the Future Elderly." R5-R17, 2005.

across the Nation on a wide variety of topics, including living with chronic conditions, maintaining optimal health, and caregiving.

ALZHEIMER'S DISEASE AND THE NEUROSCIENCE OF AGING

Alzheimer's disease is a devastating condition with a profound impact on individuals, families, the health care system, and society as a whole. Approximately 4.5 million Americans are currently battling AD, with annual costs for the disease estimated to exceed \$100 billion.² Moreover, the rapid aging of the American population threatens to increase this burden significantly in the coming decades: By 2050, the number of Americans with AD could rise to some 13.2 million, an almost three-fold increase.³

Dr. Zerhouni has told this Committee about the NIH's new paradigm for biomedical research that is "predictive, personalized, and preemptive." This vision greatly informs the NIA's comprehensive program of Alzheimer's disease research. NIA-supported investigators conduct research on topics across the spectrum of AD-related inquiry, from basic brain biology to clinical trials of potential interventions. Through these studies, we are uncovering new predictors of individual risk for AD, and using this information, along with a greater understanding of specific pathways mediating disease processes, we are developing new approaches to prevention and treatment.

Risk Factors and Early Diagnosis.—Population studies suggest that conditions affecting the circulatory system may be associated with higher risk for dementia, or that the presence of vascular disease may influence the progression of AD. One recent report indicated that AD dementia may be exacerbated by other cerebrovascular problems such as small strokes, while another linked untreated high blood pressure in mid-life with increased risk of dementia in later life. The possible association of diabetes, insulin resistance, and AD is garnering increased attention as well; recent findings from at least four long-term studies link diabetes with decline in cognitive function. The NIA recently funded two clinical trials to examine directly whether diabetes-related interventions might be effective in preventing or delaying cognitive decline or development of Alzheimer's disease.

Research suggests that the earliest AD pathology begins to develop in the brain long before clinical symptoms yield a diagnosis; the ability to make an accurate early diagnosis of AD would be highly beneficial. Improvements in brain imaging, coupled with the development of more sensitive cognitive tests, are enabling us to diagnose AD in the research setting with greater precision than ever before. Imaging techniques may become important for a number of other reasons, particularly in helping investigators understand events unfolding in specific regions of the brain in the very early stages of Alzheimer's disease and in assessing the effectiveness of potential therapeutic strategies. To speed both the development of imaging techniques and the discovery of biological markers to detect Alzheimer's disease, the National Institute on Aging and other Federal partners, in conjunction with nine pharmaceutical/biotech companies, the Institute for the Study of Aging, and the Alzheimer's Association, announced the Alzheimer's Disease Neuroimaging Initiative in October 2004. The study will test whether serial MRI, PET, or other biological markers can be used in conjunction with clinical and neuropsychological assessment to measure earlier and with greater sensitivity the development and progression of mild cognitive impairment (MCI) and early Alzheimer's disease. This major public-private partnership could help researchers and clinicians develop new treatments and monitor their effectiveness as well as lessen the time and cost of clinical trials. The study, which is taking place at approximately 50 sites across the United States and Canada, began recruitment in late 2005; approximately 800 people ages 55 to 90 will participate over the five years of the study.

Prevention and Treatment.—Results of a growing number of studies are suggesting that diet and exercise may have significant benefits on not only physical but also cognitive health. For example, in one recent study, researchers related fruit and vegetable consumption among 13,388 older women over a 10–16 year period to subsequent cognitive performance and found that women consuming the most green leafy vegetables experienced slower decline than women consuming the least amount. Long-term epidemiologic studies now also suggest that exercise may have a specific influence on aspects of cognitive decline, and researchers are hoping that

²Data from the Alzheimer's Association. See also Ernst, RL; Hay, JW. "The U.S. Economic and Social Costs of Alzheimer's Disease Revisited." *American Journal of Public Health* 1994; 84(8): 1261–1264. This study cites figures based on 1991 data, which were updated in the journal's press release to 1994 figures.

³Hebert, LE et al. "Alzheimer Disease in the U.S. Population: Prevalence Estimates Using the 2000 Census." *Archives of Neurology* August 2003; 60 (8): 1119–1122.

clinical trials will be able to directly test the therapeutic value of exercise and diet for improved cognitive performance and, eventually, for reduced risk of AD. Small clinical trials currently are ongoing to test the effects of exercise on cognitive decline, both in older adults with normal cognition and in persons with mild cognitive impairment with memory decline; a larger trial that would include a cognitive component is in the planning stages. In addition, the planned Lifestyle Interventions and Independence for Elders (LIFE) study, which has been designed to determine whether physical exercise is effective for preventing major mobility disability or death, will include a cognitive component. Clinical trials are also ongoing to test the effects of a variety of dietary supplements, including antioxidants and alpha-lipoic acid, on cognition.

Investigators are also searching for drugs that will be effective in stopping the progression of AD or, ultimately, preventing the disease altogether. Recently, investigators announced the discovery of the first agent shown to delay the clinical diagnosis of Alzheimer's in people with amnesic mild cognitive impairment, an MCI subtype strongly correlated with the later development of AD. The investigators found that individuals who took the drug donepezil (Aricept®) were at reduced risk of progressing to a diagnosis of Alzheimer's disease during the first year of the trial, but by the end of the three-year study there was no benefit from the drug. Although donepezil's effects were limited, the results are nonetheless encouraging. And although too little is known about donepezil's long-term effects to support a recommendation for its routine use to forestall the diagnosis of AD in people with mild cognitive impairment, these findings do suggest that chemoprevention of AD is possible and support our hope that future clinical studies will lead to more significant progress.

OTHER AGING-RELATED RESEARCH

Diseases of aging continue to affect many older men and women, seriously compromising their quality of life. Diseases and conditions currently under study at the NIA include:

Obesity.—Overweight and obesity are widespread in the United States and are associated with an array of health problems, including heart disease, stroke, osteoarthritis, adult-onset diabetes, certain types of cancer and physical disability. NIH has assigned a high priority to research on obesity.

These activities range from basic research on the genetic and biological mechanisms of overweight and obesity to human intervention studies. For example, recent studies of *C. elegans*, tiny worms frequently used for genetic studies, are providing important insights about fat regulation and storage that may that may be applicable in humans. NIA-supported researchers used RNA interference (RNAi), a technique in which genes are inactivated one at a time to determine their function, to screen the worm's genome and found some 417 genes involved with fat regulation and storage. Many of the genes they found have human counterparts, a number of which had not been previously implicated in the regulation of fat storage. The genes identified in *C. elegans* may ultimately suggest new targets for treating human obesity and its associated diseases.

Research has also shown that many of the disabling conditions affecting older people could be diminished through regular exercise and that fitness affects mortality risk regardless of an individual's body fat. One study, which followed men 30–83 years of age for an average of eight years, found that within each category of body fatness, “fit” men—as measured by exercise testing—were at a lower risk of death. In addition, among fit men, obesity was not significantly related to risk of death. In another study, low fitness increased mortality risk in men approximately fivefold for cardiovascular disease and threefold for all-cause mortality. Low fitness was associated with higher mortality in all weight groups.

At a 2004 NIA and Centers for Medicare and Medicaid Services (CMS) sponsored workshop, researchers used published findings and trends to postulate that if the United States were able to prevent obesity until a person reaches 65 years of age by adjusting the body mass index for all cohorts entering Medicare, we could realize a significant decline in the percent with heart disease and diabetes, a significant increase in the percent without disability, and a cost savings to Medicare on the order of \$10 billion annually over the subsequent 30 years.⁴

⁴Lakdawalla, DN et al. The Health and Cost Consequences of Obesity Among the Future Elderly. Health Affairs on line special issue “Health and Spending of the Future Elderly.” R30–41.

Heart disease.—Each year over 1 million Americans undergo angioplasty,⁵ a procedure in which a long, thin tube attached to a tiny balloon is used to access and widen a blood vessel at the site of narrowing or blockage. However, a significant number of these individuals go on to experience restenosis, or gradual narrowing of the artery at the site of the blockage; this condition is aggravated by the implanting of stents (tiny metal scaffolds placed inside the artery to hold it open). Restenosis usually occurs within six months of angioplasty and results from the migration of cells from the middle of the arterial wall into the inner layer of the artery, where they multiply and block normal blood flow. Recognizing that cell division is crucial to the development of restenosis, NIA scientists tested the anticancer drug paclitaxel (Taxol®), which arrests cell division, as a means of preventing the tissue growth that leads to vessel narrowing, and found that stents coated with paclitaxel can delay restenosis both safely and effectively. The investigators obtained a patent for these paclitaxel-coated stents, and a cooperative research and development agreement was established with private industry partners to begin clinical testing. Today, paclitaxel is one of only two drugs that, when applied to stents, have been shown to safely reduce the incidence of restenosis in humans. FDA approval of paclitaxel-coated stents was granted in March 2004, and currently over 70 percent of the drug-eluting stents used worldwide are paclitaxel-coated. Approximately 1.8 million patients worldwide have received paclitaxel-coated stents to date.

Diabetes.—NIH investigators searching for potential treatments for type 2 diabetes conducted a study of the compound exendin-4, an analog of a hormone that is naturally released after eating and that can lower blood sugar in people with diabetes. The investigators found that exendin-4 is safe and effective, and in April 2004, the Food and Drug Administration approved exenatide (Byetta™), a synthetic derivation of exendin-4, for the treatment of type 2 diabetes.

HEALTH COMMUNICATIONS AND PROMOTION

The NIHSeniorHealth website continues to be a major initiative that enables the growing number of “wired seniors” to find credible aging-related health information in an online format that is compatible with their cognitive and visual needs, as evidenced by NIH-supported research. Conceived by NIA and jointly developed with the National Library of Medicine (NLM), the website now includes 26 health topics developed by eleven NIH Institutes. Each month, 52,000 unique visitors browse over a half a million pages. NIHSeniorHealth serves as a model for web designers seeking to make sites accessible to older adults. To increase the number of older adults skilled in searching for health information online, NIA has developed and is evaluating a senior-friendly Internet training curriculum geared around NIHSeniorHealth and NLM’s MedlinePlus web site for those who train older individuals to use computers.

Changes in public health policy may necessitate the development of new communications strategies and techniques targeted at older Americans, as was demonstrated with the passage of Medicare Part D, the “prescription drug benefit” for U.S. seniors. NIA-supported researchers are currently using established datasets to rapidly collect information and analyze patterns of use under Medicare Part D; their findings have been communicated to the CMS on an ongoing basis and will inform the creation of new strategies for tailored communications that will assist older Americans in understanding and maximizing use of this important new program.

Thank you for the opportunity to testify before this Subcommittee. I would be happy to answer any questions you may have.

PREPARED STATEMENT OF DR. SHARON HRYNKOW, ACTING DIRECTOR, FOGARTY INTERNATIONAL CENTER

Mr. Chairman and Members of the Committee: I am pleased to present the fiscal year 2007 President’s Budget for the Fogarty International Center (FIC). The fiscal year 2007 budget includes \$66,681,000, which reflects an increase of \$303,000 over the fiscal year 2006 enacted level of \$66,378,000 comparable for transfers proposed in the President’s request.

Forty-seven years ago, Congressman John E. Fogarty noted, “Time and time again, it has been demonstrated that the goal of better health has the capacity to demolish geographic and political boundaries and to enter the hearts and minds of men, women, and children in the four corners of the earth. It is an issue which serves as a forceful reminder of the oneness, the essential brotherhood of man.” Congressman Fogarty, the visionary namesake of the National Institutes of Health’s

⁵Data from the National Heart, Lung, and Blood Institute.

(NIH's) John E. Fogarty International Center for Advanced Study in the Health Sciences (Fogarty), recognized that when it comes to disease, we are truly one world. His words and those of his Congressional colleagues implored us to work for "a healthy America, in a healthier world."

Today, Fogarty works to meet this goal in two ways: by supporting the whole of the NIH mission via international partnerships, and through the support of global health research and training programs aimed at improving the health of citizens in the United States and around the globe. As a nation, our interest in global health stems not only from humanitarian concerns, but also from an enlightened self-interest. Such interests involve protecting our nation from imported diseases, and political and economic considerations—healthy, stable countries make strong allies and trading partners. In addition, through partnerships with scientists from around the world, we are able to identify new strategies and new understandings of disease processes, including HIV/AIDS, tuberculosis, and chronic diseases such as heart disease, that affect us all. I welcome this opportunity to relate Fogarty's progress over the past year and proposed plans for fiscal year 2007. While Fogarty's programs span over 20 topical areas, I will focus on three exemplars in this summary.

THE BATTLE AGAINST HIV/AIDS

Fogarty continues to place a high priority on combating HIV/AIDS the deadliest pandemic of modern times. According to UNAIDS, an estimated 4.9 million people worldwide became newly infected with HIV in 2004—the highest number of new cases reported in any single year since the beginning of the pandemic. As the United States works to combat the spread of AIDS domestically and globally, trained scientists in countries hard-hit by AIDS are crucial allies in our fight. In the 18-year history of Fogarty's flagship AIDS program, the AIDS International Research and Training Program (AIRTP), Fogarty has helped train 2,000 health scientists, including Ph.D. and Masters level researchers from developing countries working on AIDS. More than 50,000 have received short-course training in their home countries through this program. These scientists represent a substantial increase in the global capacity to fight AIDS and provide a wealth of allies in our international struggle.

Haiti has the largest number of people living with AIDS in the Caribbean. For almost two decades, Fogarty has invested in research and public health infrastructure to combat the HIV/AIDS crisis there. Haiti has now begun to "turn the corner on AIDS," according to Dr. Jean Pape, Haiti's leading AIDS researcher and long-standing Fogarty collaborator. As a result of Fogarty's work and that of partner agencies, HIV seroprevalence at a key sentinel site in Haiti dropped from 6.3 percent in 1993 to 2.9 percent in 2003.

Due to this strong research base, Dr. Pape's institution received a grant from the President's Emergency Plan for AIDS Relief (PEPFAR), allowing 2,000 patients to receive antiretroviral therapy. An analysis of the first 1,000 patients at the one-year follow-up indicates outcomes comparable to those achieved in the United States in terms of survival; other indicators show reduced amounts of HIV in the blood of AIDS patients, as well as increased amounts of cells that are critical to staving off the impacts of HIV. None of this would have been possible without the vision and foresight of Fogarty, working hand in glove with NIH partners, including the National Institute of Allergy and Infectious Diseases.

In fiscal year 2007, Fogarty plans to expand both major AIDS programs in its portfolio. The AIRTP expansion would involve new U.S. universities, including minority institutions, important partners as we work to address global health challenges and the range of U.S. challenges on AIDS. In addition, Fogarty's new training program in clinical, operational and health services research would be expanded to build much needed capacity expertise in monitoring and evaluating AIDS programs abroad.

ADDRESSING THE THREAT OF EMERGING AND RE-EMERGING INFECTIOUS DISEASES: PREDICTION AND PREEMPTION

Little is known about the ecological factors that lead to the emergence or re-emergence of infectious diseases, including potentially pandemic diseases such as avian flu. We do know that most new diseases come from animals, both wild and domesticated. But beyond that we have little ability to predict the emergence of new diseases, or how new or existing diseases spread among animals, and from animals to humans. To better understand the relationships between ecological factors that drive emergence and transmission of infectious agents, and to develop predictive models that would suggest practical modes to interrupt disease spread, Fogarty led the development of a unique interagency program on the Ecology of Infectious Dis-

eases (EID). The EID program fills a critical gap in our national effort to protect the health of the public—both in the United States and globally—against the threat of epidemic and emerging infectious diseases. The program links microbiologists, veterinarians, physicians, ecologists, geospatial scientists, and mathematical modelers together into transdisciplinary teams to create new knowledge and new methods to predict and prevent the spread of infectious disease. In its first years of operation, the EID program has already linked experts from 23 countries and has supported publication of over 200 scientific articles on dozens of human and wildlife diseases, including schistosomiasis, Hanta virus, cholera, and severe acute respiratory syndrome (SARS).

SARS was first reported in southern China in the winter of 2002–2003, and within a few months it had spread to over two dozen countries. Within a month of its discovery, SARS was recognized as a viral respiratory illness caused by a newly identified coronavirus (CoV), yet the origin of the virus and how it was initially transmitted to humans remained a mystery. Preliminary evidence suggested that the palm civet (a raccoon-like mammal common in live animal markets in southern China) might have spread the virus to humans. However, the occurrence of related viruses in bats led some to think these animals may have been involved. A team of Fogarty-funded researchers from the United States, China, and Australia collected and analyzed specimens from nine species of bats in their native habitats in southern China. The team studied the presence of antibodies to the SARS virus and performed genome sequencing of viral isolates from positive tissues, comparing these genome sequences to that of the SARS virus. Study results indicate that bats are the natural reservoir of the SARS virus, suggesting that palm civets played an intermediary role in human infections. These findings have major implications for development of public health strategies to combat the spread of SARS. In fiscal year 2007, FIC expects to expand the EID program in terms of the number of projects supported and their scope, simultaneously increasing the focus on supporting translation of research findings and predictions into action.

As we consider the daunting challenge of pandemic avian influenza, programs such as the EID can provide a critical component in our ability to predict and prevent emergence and transmission of this and other disease threats. The United States and its global partners will be better poised to make effective interventions to prevent the spread of avian flu through understanding of migration patterns of reservoir bird species, the interactions between humans, domestic animals and birds, and the pathogen dynamics in and among these hosts. We cannot predict the spread of this disease, in its current zoonotic form, using mathematical or statistical models if we do not support the fieldwork necessary to sample wild and domesticated birds (work done by ornithologists, veterinarians, and ecologists). The field data are useful only for post field analysis if we integrate them into predictive models. The interagency EID program is unique in its integration of these methods into interdisciplinary teams to understand the biology and predict disease emergence and transmission.

THE GLOBAL BURDEN OF TRAUMA AND INJURY

According to the World Health Organization (WHO), the numbers and the global burden due to trauma and injury are on the rise: more than 1.2 million people are killed in traffic accidents annually, and up to 50 million more are injured or disabled. If current trends continue, the number of people killed and injured on the world's roads will rise by more than 60 percent between 2000 and 2020. Almost 90 percent of deaths due to injuries take place in poorer countries—this is true for all forms of such trauma including road accidents, war, homicides, and suicides. And, according to the Association for Safe International Road Travel, road traffic accidents are the second leading cause of death for Americans abroad.

To address this growing challenge, Fogarty, working closely with the Centers for Disease Control and Prevention, WHO, the Pan American Health Organization, and eight other NIH institutes, initiated a research training program to build the capacity of developing country investigators and institutions to conduct human trauma and injury research. The International Collaborative Trauma and Injury Research Training (ICTIRT) program involves collaborators from United States and developing country institutions to train the next generation in basic and applied science, the epidemiology of risk factors, acute care and survival, rehabilitation, and the long-term mental health consequences of trauma and injury, including civil strife. Benefits of this program will accrue not only to developing countries but, as low-cost and effective strategies are identified, to communities around the world. This program was initiated with awards in fiscal year 2005 and fiscal year 2006. We anticipate new awards in fiscal year 2006 and fiscal year 2007.

CONCLUSION

The programs and international initiatives of the Fogarty International Center are a living testament to the vision of Congressman John E. Fogarty. As we consider the daunting global challenges of AIDS, avian influenza and chronic problems, including obesity and mental health disorders, we understand the interconnectedness of the United States and the global community. These challenges require us to move forward with efficiency and diplomacy, for the benefit of the American people and the global community.

PREPARED STATEMENT OF DR. THOMAS R. INSEL, DIRECTOR, NATIONAL INSTITUTE OF MENTAL HEALTH

Mr. Chairman and members of the Committee: I am pleased to present the fiscal year 2007 President's budget request for the National Institute of Mental Health (NIMH). The fiscal year 2007 budget includes \$1,394,806,000, which reflects a decrease of \$8,709,000 under the 2006 enacted level of \$1,403,515,000 comparable for transfers proposed in the President's request. In my statement, I will call to your attention our Nation's most prevalent mental and behavioral disorders and include a brief review of our research activities and accomplishments.

THE BURDEN AND COST OF MENTAL ILLNESS

Mental disorders are common, chronic, and disabling. They cause more disability than any other class of communicable medical illness in American adults under age 45, according to the World Health Organization's Global Burden of Disease report. The National Comorbidity Survey Replication (NCS-R), funded by NIMH and released in May 2005, documents the prevalence and severity of specific mental disorders in the United States. The study shows that half of all lifetime cases of mental illness begin by age 14, making these the chronic diseases of the young. About 6 percent of the U.S. population is afflicted with a severely disabling mental disorder in a given year. Most troubling, this landmark study has demonstrated that despite effective treatments, there are long delays—sometimes decades—between first onset of symptoms and when people seek and receive treatment.

The cost in human suffering from these mental diseases is compounded further by their economic burden. According to the President's New Freedom Commission on Mental Health (2003), individuals with serious mental illnesses represent the single largest diagnostic group (35 percent) on the Supplemental Security Income (SSI) rolls. Medicaid is the largest single payer of mental health services, with more than 50 percent of all mental health expenditures paid for by the public sector (including Medicaid, Medicare, state and local governments).

The good news is that there now are some extraordinary new tools and technologies, such as neuroimaging and genomics, with which to address these urgent public health needs. Our major challenge is to integrate and translate basic research discoveries and technological advances into practical strategies that can help all communities, including children, the socioeconomically disadvantaged, and others facing barriers to mental health care.

ENVISIONING PERSONALIZED CARE

Research efforts stemming from former President George Bush's proclamation of the 1990s as the Decade of the Brain established that mental disorders (autism, bipolar, depression, schizophrenia, and others) are brain disorders. The current decade is one in which many major candidate molecules, cells, and circuits for normal and abnormal brain function are being identified for the first time. Through these discoveries research will definitively identify the specific brain pathways that underlie each of the major mental disorders. By identifying the features of the brain that go awry in mental illnesses, we will have clear new targets to test how biological, behavioral, and environmental factors affect illness and to develop more effective interventions with the ultimate vision of delivering personalized care through pre-emptive treatments and strategic preventions.

Currently, there are effective treatments for many mental disorders such as depression and anxiety disorders. Studies show that even from a business standpoint, treating these disorders is highly cost-effective; national business groups are encouraging employers to support such treatments in order to reduce healthcare costs while also improving productivity and reducing absenteeism.

Not all treatments work for everyone, however, and clearly there remains room for improvement in both diagnosis and treatment. In mental disorders, just as in the rest of medicine, diagnosis should rely on detection of biomarkers of the specific

disease, and treatments should be based on medication and/or behavioral interventions targeting specific brain regions and processes. For a person with mental illness, one can imagine that a future clinician would use a cognitive task together with neuroimaging and genetics to diagnose and select a specific treatment, just as a contemporary cardiologist uses a stress test and echocardiogram to diagnose ischemic heart disease and select the proper intervention.

It is critical to realize that this vision does not mean designing exotic technologies for a few privileged patients. The ultimate goal is personalized or individualized care for a broad spectrum of people with mental disorders. Now, specific treatments for any given patient are largely developed through trial and error. As researchers learn more about the brain pathophysiology of mental disorders and related behavioral and environmental factors, treatments will become more specific. Early detection of mental illnesses will require a thorough understanding of the range of risks that affect brain processes, which in turn is based on a comprehensive understanding of genetics and experience.

PRACTICAL CLINICAL TRIALS

As noted above, we have treatments that are helpful for nearly all of the mental disorders. But these treatments are not optimal; recovery is often slow, incomplete, and compromised by adverse effects. Since we do not know who will respond completely and who will develop adverse effects, each clinician depends on trial and error with each patient. The Institute has developed practical clinical trials in more than 10,000 patients to help clinicians individualize treatments. Practical clinical trials, or “effectiveness studies,” are designed to examine changes in symptoms and functioning, changes which are vital to determining whether a treatment improves quality of life, caregiving burden, or health service use. The designs of practical clinical trials help increase relevancy to real-world clinical practice to help clinicians answer the question: what is the best treatment for my patient? Each of the following NIMH-funded practical clinical trials provides results from the largest and longest studies of their kind.

In the Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE) Study, 1,432 schizophrenia patients from 56 sites, including private practices, community health care centers, and state facilities, were randomly assigned to treatment with one of five medications for 18 months. In the first phase of analysis the study found that newer, “atypical” antipsychotics are not much more effective than older, conventional antipsychotics; however all the medications studied have unique side effect profiles, some of which include significant weight gain and metabolic side effects, thus increasing risk for diseases such as diabetes. Later phases of this study will examine crucial issues including effects of switching from one treatment to another, use of health services, and cost-effectiveness.

Another example is the Treatment for Adolescents with Depression Study (TADS), which compared short- and longer-term effectiveness of medication and psychotherapy for depression in 439 adolescents. TADS was designed to test best-practice care for depression and was carried out by 13 academic and community clinics across the country. Researchers found that fluoxetine (a selective serotonin reuptake inhibitor) in combination with cognitive behavioral therapy was more effective against adolescent depression than either one alone. In addition, clinically significant suicidal thinking was greatly reduced in all four treatment groups, with those receiving medication combined with cognitive therapy showing the greatest reduction. This is an especially important finding, considering recent concerns that the use of antidepressant medications themselves may induce suicidal behavior in youths. This study shows that treatment leads to a significant improvement of depression overall. It is vital that all patients being treated for depression be closely monitored.

The Sequenced Treatment Alternatives to Relieve Depression Trial (STAR-D) examines 4,041 adults with major depression, particularly those who previously showed poor outcomes to treatment, to see if switching medications or augmenting the initial drug be more likely to achieve a remission. The study, conducted at 41 sites coordinated by 14 regional centers, will also answer how the side effects of the various medications compare and how psychotherapy compares with medication for treatment-resistant depression.

In the Systematic Treatment Enhancement Program for Bipolar Disorder (STEP-BD) trial, 4,360 participants with bipolar disorder from 20 private, state, and community practice sites underwent various treatment pathways to find the most effective long-term and acute treatments and ways to prevent relapse. In the first phase, slightly more than half of the first group of 1,469 participants (58 percent) achieved recovery. In addition, almost half of the recovery group had a recurrence during the

follow-up period, and the majority (70 percent) of recurrences was characterized by a return to a depressive state. In the following phases of the trial, not yet published, various treatments will be tried such as mood-stabilizing medications, antidepressants, atypical antipsychotics, and various “talk” therapies, to see which is best for acute treatment, long-term treatment, and prevention of relapse.

NIMH INITIATIVES FOR FISCAL YEAR 2007

To further advance the vision of personalized mental health care, NIMH will pursue two collaborative initiatives in fiscal year 2007. The first is the Autism Phenome Project, in collaboration with the NIH Autism Coordinating Committee, the Centers for Disease Control and Prevention, and the Department of Energy. Just as the Human Genome Project identified the sequence and organization of human DNA, the phenome project seeks to identify the various clinical characteristics (phenotypes) and subtypes of autism and autism spectrum disorders. Identifying specific phenotypic subtypes will aid research on genetic and other potential causes and suggest more specific approaches to treatment.

The second collaborative initiative is with the Department of Defense (DOD) and the Department of Veterans Affairs (VA) to study the mental health needs of active duty, National Guard, and Reserve personnel including their transition to VA health services. In particular, representative groups of men and women will be studied over time to assess post-deployment adjustment difficulties (including post-traumatic mood and anxiety disorders, and substance use and abuse disorders), the development and effectiveness of early detection and intervention methods, and the possibility of decreasing the risk of developing chronic conditions, disability, and death in those with adjustment difficulties.

These initiatives, in conjunction with the exciting research already underway, will enable NIMH to make significant gains in the upcoming years. We intend to realize our vision of translating basic research and technologies to improved diagnosis, treatment, and preventive strategies that will allow development of personalized mental health care for the millions of Americans affected by mental illnesses.

PREPARED STATEMENT OF DR. STEPHEN I. KATZ, DIRECTOR, NATIONAL INSTITUTE OF ARTHRITIS AND MUSCULOSKELETAL AND SKIN DISEASES

Mr. Chairman and Members of the Committee: I am pleased to present the fiscal year 2007 President's budget request for the National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS). The fiscal year 2007 budget includes \$504,533,000, a decrease of \$3,399,000 below the fiscal year 2006 enacted level of \$507,932,000.

The NIAMS was created by an Act of Congress nearly 20 years ago, and since its inception, the Institute has contributed to significant research progress in areas of public health importance across diseases that are common, costly, and have a major impact on quality of life, disability, and mortality. Research milestones in the history of the Institute include the development of life-saving treatments for kidney failure in patients with lupus, and ground-breaking work to uncover the genetic bases of periodic fever syndromes that affect both children and adults, among many others.

Most recently, investments that NIAMS made as a result of the NIH budget doubling are bringing results that will directly benefit patients. These include support for large-scale clinical trials in areas of high public health impact, such as osteoporosis and back pain; efforts in biomarkers research and epidemiology studies for common conditions such as osteoarthritis, as well as uncommon, but often devastating, disorders such as scleroderma; and new initiatives in translational research for diseases such as muscular dystrophy. Looking to the future, NIAMS will continue its commitment to fund outstanding science across a broad spectrum to enable us to better understand, treat, and, ultimately, prevent diseases of the bones, joints, muscles, and skin.

PREVENTIVE MEDICINE

The NIAMS has made significant investments in studies to identify risk factors and biomarkers of disease, in an effort to facilitate the early identification of signs and symptoms, and to develop interventions that are more effective. This is particularly important from a public health perspective for common conditions such as osteoporosis and osteoarthritis that already afflict tens of millions of Americans, and will affect even more as the U.S. population ages in the coming decades.

In the area of osteoporosis, the NIAMS, along with the National Institute on Aging, has provided steady support for the Study of Osteoporotic Fractures (SOF), a multi-site clinical investigation to determine the risk factors for osteoporotic fractures in older women. Begun in 1986, SOF scientists recruited 9,704 white women aged 65 and older from 4 metropolitan areas for this study. In 1997, an additional 662 African American women who are now seen with the original cohort were enrolled. Major contributions from this long-term study include the findings that bone mineral density (BMD) of the hip is the best predictor of all types of fractures, and that weight loss and parental history of hip fractures are among the most important risk factors for this condition. SOF investigators have also learned that the relationship of BMD and fracture risk is similar in white and African American women, but that at every level of BMD, fracture rates are 30 to 40 percent lower in African American women. These insights are providing clinicians with important information about which women are at most risk for this debilitating disease, so that prevention strategies may be used more effectively. Similar epidemiological studies have now been launched to learn about risk factors for osteoporosis in men.

With respect to osteoarthritis, the NIAMS partnered with the National Institute on Aging, several other NIH components, and four pharmaceutical companies in establishing the Osteoarthritis Initiative, a public-private partnership aimed at developing clinical research resources that support the discovery and evaluation of biomarkers and surrogate endpoints for osteoarthritis clinical trials. For the first time, a public-private partnership is bringing together new resources and commitments to help find biological markers for the onset and progression of osteoarthritis. Recruitment of participants is actively underway, and by the end of fiscal year 2005, more than 3,800 participants have been recruited. One year follow-up measurements have been carried out on over 1,000 participants, and will continue for the next 4 years. All data and images collected will be available to researchers worldwide to help quicken the pace of scientific studies and biomarker identification. This consortium serves as a model for future endeavors that link the public and private sectors.

COMPLEX GENETICS

The NIAMS is taking full advantage of the explosion of information related to genetics, genomics, and proteomics to pursue the causes of complex diseases, and how best to treat them. This includes recent work which identified a genetic variation that doubles the risk of developing rheumatoid arthritis. Scientists have long suspected that autoimmune diseases such as rheumatoid arthritis result from a combination of genetic and environmental factors. Now, a NIAMS-funded research team has identified a specific genetic variation, called a single nucleotide polymorphism or SNP, that increases rheumatoid arthritis risk twofold. The SNP is located within a gene that codes for a particular enzyme that is known to be involved in controlling the activation of white blood cells, called T cells, that play an important role in the body's immune system. Under normal conditions, the enzyme works as a negative regulator: it inactivates a specific signaling molecule which, in turn, interrupts the communications and keeps immune cells from becoming overactive. However, in cases where the SNP is present in one or both copies of a person's genes for this enzyme, the team found that the negative regulation by the enzyme appears to be inefficient, allowing T cells and other immune cells to respond too vigorously, causing increased inflammation and tissue damage. The implications of this finding go beyond a better understanding of rheumatoid arthritis risk. It may also help explain why different autoimmune diseases tend to run in families, since this gene variant is also found in diabetes and lupus.

In other efforts, researchers have recently made breakthroughs in understanding the genetics underlying psoriasis, a chronic skin disease characterized by scaling and inflammation. This disorder occurs when skin cells rapidly pass from their origin below the surface of the skin and pile up on the surface before they have a chance to mature. Usually this movement (also called turnover) takes about a month, but in psoriasis it may occur in only a few days. Recent studies funded by the NIAMS are helping scientists and doctors to understand the disease process at the molecular level, and what role genes play in predisposing people toward psoriasis. In one such project, researchers investigated the role of both genes and the environment in psoriasis, psoriatic arthritis, and atopic dermatitis, another inflammatory skin condition. The researchers found similarities in genetic susceptibility for psoriasis and atopic dermatitis. As for psoriatic arthritis—a condition in which inflamed joints produce symptoms of arthritis for patients who have or will develop psoriasis—they found that the presence of modifier genes can indicate which people with psoriasis are also at risk for psoriatic arthritis.

TRANSLATIONAL RESEARCH

A key ingredient in research success is translation: work to bring insights from the laboratory bench to the patient bedside, and back again, with the ultimate goal of improving patient care and public health. In this vein, NIAMS has recently launched a new program to bring together basic and clinical scientists in a targeted and organized way. The Centers of Research Translation (CORT) program emphasizes the translation of results from basic to clinical studies, as well as translating findings from clinical research to enhance and focus the approaches used in basic studies—all with the goal of improving public health.

This commitment to translational research is bringing results in many areas, including the field of muscular dystrophy research. NIAMS supports two of the six Senator Paul D. Wellstone Muscular Dystrophy Cooperative Research Centers: the first, at the University of Pittsburgh, focuses on gene and stem cell therapies to treat muscle disease; and the second, located at the University of Pennsylvania, is examining strategies to inhibit muscle degeneration and promote muscle growth. These centers promote side-by-side basic, translational, and clinical research; provide resources that can be used by the national muscular dystrophy and neuromuscular communities; and provide training and advice about muscle diseases for researchers and clinicians.

The Institute has also launched new initiatives to encourage translational research in all forms of muscular dystrophy, and to stimulate career development opportunities for muscle disease researchers. These efforts are designed to facilitate the development of new and more effective treatments for muscular dystrophy, and to increase the number and quality of investigators in basic, translational, and clinical research focused on this disease.

REGENERATIVE MEDICINE

Regenerative medicine—a multidisciplinary field that involves the life, physical, and engineering sciences—is an emerging area of research that cuts across several NIAMS programs. For example, important advances have been made recently in the development of promising new polymers for cartilage repair. Cartilage is a tissue that lacks capacity for self-repair. However, multidisciplinary studies by biologists, engineers, physicians, and other are providing new strategies for treating degenerative cartilage that may result in treatments for articular cartilage lesions. Researchers funded by the NIAMS have developed a class of injectable materials based on a biodegradable polymer, OPF (oligo-polyethylene glycol fumarate), for cartilage tissue engineering. Short-term studies in experimental animals demonstrated excellent tissue filling and integration resulting from implantation of these materials into cartilage defects. The polymers were also designed to deliver bioactive molecules (such as growth factors) as well as cells (such as chondrocytes or progenitor cells) to cartilage lesions to enhance tissue repair. Early results show that chondrocytes remain viable, proliferate, and synthesize cartilage matrix components in these polymer gels. Taken together, these results indicate that OPF gels are promising materials for cell delivery in cartilage repair strategies.

CONCLUSION

The scientific advances and innovative initiatives highlighted above paint a picture of research progress that has benefited millions of American children and adults. In the coming fiscal years, NIAMS will focus on strategic collaborations by building partnerships to pursue shared goals across public, academic, and private research entities. A primary example of such a coordinated effort is the Collaborative Initiative on Bone Strength. NIAMS—in conjunction with other NIH components, the Food and Drug Administration, and industry partners—is exploring a potential public-private collaboration on bone strength. The main goals of such an initiative would be to provide data supporting the use of new bone strength markers as surrogate endpoints for fractures in clinical trials, and to find measurements that predict risk of fracture more accurately than does bone density. This would facilitate the continued development and approval of new treatment alternatives to prevent fractures through the support of clinical trials that are smaller, shorter, and less expensive than current studies.

Finally, NIAMS is placing a high priority on strengthening the pipeline of well-trained investigators across the Institute's areas of research interest. This commitment includes funding for the new NIH award program, "Pathway to Independence," to support young investigators, as well as an enhanced emphasis on basic, translational, and clinical training at the major research centers supported by NIAMS. All of these activities are driven by our dedication to fulfill the mandate

that Congress gave the Institute when it created NIAMS; namely, to reduce the burden of illness and to enrich the quality of life for all Americans affected by diseases within our mission.

PREPARED STATEMENT OF RAYNARD KINGTON, DEPUTY DIRECTOR, OFFICE OF THE DIRECTOR

Mr. Chairman, Members of the Committee: I am pleased to present the fiscal year 2007 President's budget request for the Office of the Director (OD). The fiscal year 2007 budget includes, \$667,825,000, an increase of \$140,259,000 over the fiscal year 2006 appropriation of \$527,566,000 comparable for transfers proposed in the President's request. The OD provides leadership, coordination, and guidance in the formulation of policy and procedures related to biomedical research and research training programs. The OD also is responsible for a number of special programs and for management of centralized support services to the operations of the entire NIH.

The OD guides and supports research by setting priorities; allocating funding among these priorities; developing policies based on scientific opportunities and ethical and legal considerations; maintaining peer review processes; providing oversight of grant and contract award functions and of intramural research; communicating health information to the public; facilitating the transfer of technology to the private sector; and providing fundamental management and administrative services such as budget and financial accounting, and personnel, property, and procurement management, administration of equal employment practices, and plant management services, including the implementation of environmental and public safety regulation. The principal OD offices providing these activities include the Office of Extramural Research (OER), the Office of Intramural Research (OIR), and the Offices of: Science Policy; Communications and Public Liaison; Legislative Policy and Analysis; Equal Opportunity; Budget; and Management. This request contains funds to support the functions of these offices. In addition, the OD also maintains several trans-NIH offices and programs to foster and encourage research on specific, important health needs. I will now discuss the budget request for the OD in greater detail.

NIH ROADMAP FOR MEDICAL RESEARCH

Responding to 21st Century biomedical challenges, the NIH Roadmap for Medical Research serves as a test bed for trans-NIH programs designed to accelerate the pace and translation of biomedical discovery. Derived from stakeholder input, Roadmap initiatives are bearing fruit with infrastructure, tools and training programs that serve and intersect the needs of NIH research disciplines and missions. Several large initiatives follow a "hub-and-spoke" model that connects projects and research centers to one another and to the research community at large. For example, the National Centers of Biomedical Computing have created a networking 'hub' to cooperatively develop a number of computing resources that are being followed quickly by investigator-initiated projects (spokes) that will use and assess these resources. Recognizing that gaps in scientific knowledge can be filled in many types of ways, the Roadmap invests in people with innovative, high-risk ideas and in programs and training to foster the development of new research teams and disciplines. Re-engineering of clinical research is also underway with efforts to harmonize research policies, develop tools to examine patient-reported outcomes, integrate clinical research networks, and accelerate multidisciplinary and translational research training. The NIH Roadmap for Medical Research is lowering barriers to biomedical research and harnessing the collective knowledge from multiple disciplines to make the next great leap forward in biomedical discovery. The fiscal year 2007 budget request for NIH Roadmap for Medical Research is \$110,700,000, an increase of \$28,530,000 over the fiscal year 2006 level.

OFFICE OF AIDS RESEARCH

The Office of AIDS Research (OAR) plays a unique role at NIH, establishing a roadmap for the AIDS research program. OAR coordinates the scientific, budgetary, legislative, and policy elements of the NIH AIDS research program. Our response to the AIDS epidemic requires a unique and complex multi-institute, multi-disciplinary, global research program. Perhaps no other disease so thoroughly transcends every area of clinical medicine and basic scientific investigation, crossing the boundaries of the NIH Institutes and Centers. This diverse research portfolio demands an unprecedented level of scientific coordination and management of research funds to identify the highest priority areas of scientific opportunity, enhance collaboration, minimize duplication, and ensure that precious research dollars are invested effec-

tively and efficiently, allowing NIH to pursue a united research front against the global AIDS epidemic. OAR oversees the development of the annual comprehensive trans-NIH AIDS-related research plan and budget, based on scientific consensus about the most compelling scientific priorities and opportunities that will lead to better therapies and prevention strategies for HIV disease. The Plan serves as the framework for developing the annual trans-AIDS research budget; for determining the use of AIDS-designated dollars; and for tracking and monitoring those expenditures. OAR also identifies and facilitates multi-institute participation in priority areas of research and facilitates NIH involvement in international AIDS research activities. The fiscal year 2007 budget request for OAR is \$59,290,000, which is a decrease if \$1,000,000 below the fiscal year 2006 level.

OFFICE OF RESEARCH ON WOMEN'S HEALTH

The Office of Research on Women's Health (ORWH), the focal point for women's health research for the Office of the Director, strengthens, enhances and supports research related to diseases, disorders, and conditions that affect women, and sex/gender studies on differences/similarities between men and women; ensures that women are appropriately represented in biomedical and biobehavioral research studies supported by the NIH to facilitate analyses by sex/gender; and develops opportunities for the advancement of women in biomedical careers and investigators in women's health research. ORWH is developing a novel initiative, entitled Advancing Novel Science in Women's Health Research (ANSWHR), with the NIH ICs to support innovative research in women's health and sex/gender issues. ORWH will continue funding for new or continuing programs through new RFAs for its highly successful interdisciplinary programs: Specialized Centers on Research (SCORs) Affecting Women's Health and Building Interdisciplinary Research Careers in Women's Health (BIRCWH). Reissuance of these interdisciplinary programs will insure the continuation of advances in sex and gender factors in women's health research and the mentored development of junior faculty by bridging advanced training with research independence resulting in more clinical researchers performing in women's health research. The fiscal year 2007 budget request is \$40,949,000, which is the same as the fiscal year 2006 level.

OFFICE OF BEHAVIORAL AND SOCIAL SCIENCES RESEARCH

The NIH's long history of funding behavioral and social sciences research has contributed significantly to our understanding, treatment, and prevention of disease and to the promotion of health and well-being. To further NIH's ability to capitalize on such opportunities, Congress established the Office of Behavioral and Social Sciences Research (OBSSR) to provide leadership in developing research programs that are likely to improve our understanding of processes underlying health and disease and to provide directions for intervention. OBSSR works to ensure that behavioral and social sciences research is integrated into the greater NIH health research enterprise.

As Secretary Leavitt's announcement of the Genes, Environment and Health Initiative (GEHI) made clear, very little is known about how various characteristics of the environment interact with genetics to influence susceptibility to illness. The GEI's focus is interactions among genetics, environmental toxins and individual behaviors (dietary intake and physical activity) that influence the risk of developing a number of common diseases. Based on recommendations from an OBSSR-supported Institute of Medicine study examining the state of the science on gene-social environment interactions, OBSSR is collaborating with ICs to develop research initiatives at the interface of social and genetic factors and health. Moreover, the office is initiating training institutes in genetics for behavioral and social scientists to provide them with the expertise they need to function in interdisciplinary research teams working in this area.

Another area of trans-NIH emphasis has been effective design, communication and implementation of health and clinical information to ensure optimal outcomes across groups of diverse stakeholders. OBSSR's participation in the "Dissemination and Implementation Research in Health" program will help identify and overcome many barriers to the widespread adoption of evidence-based social and behavioral interventions to treat and prevent illness. The promise of these efforts lies in their potential to improve treatment and prevention of illness, the use of these tools to address disparities in health outcomes, and the possibility of demonstrating opportunities for more cost-effective health policy and practice.

To continue such groundbreaking work in the behavioral and social sciences, the fiscal year 2007 budget request for OBSSR is \$26,121,000, the same amount as the fiscal year 2006 level.

OFFICE OF DISEASE PREVENTION

The primary mission of the Office of Disease Prevention (ODP) is to stimulate disease prevention research across the NIH and to coordinate and collaborate on related activities with other federal agencies as well as the private sector. There are several other offices within the ODP organizational structure.

The Office of Medical Applications of Research (OMAR) has as its mission to work with NIH Institutes, Centers, and Offices to assess, translate and disseminate the results of biomedical research that can be used in the delivery of important health interventions to the public. The ODP has two additional specific programs/offices that place emphasis on particular aspects of the prevention and treatment of disease the Office of Dietary Supplements (ODS) and the Office of Rare Diseases (ORD).

In fiscal year 2007, the ODS requests a budget of \$26,807,000, the same amount as the fiscal year 2006 level. ODS promotes the scientific study of the use of dietary supplements by supporting investigator-initiated research, and stimulating research through the conduct of conferences and presentations at national and international meetings. Other current ODS efforts include:

- Sponsorship of systematic reviews on the efficacy and safety of dietary supplements in reducing the risk of chronic diseases such as cancer and heart disease.
- Collaborations for the development, validation, and dissemination of analytical methods and reference materials for dietary supplements.
- Support for and development of databases of dietary supplement information including:
 - National Health and Nutrition Examination Survey (NHANES);
 - Collaboration with USDA to develop an analytically-based database of dietary supplement ingredients;
 - Plan to develop a dietary supplement label database;
 - International Bibliographic Information on Dietary Supplements (IBIDS);
 - CARDS, a database of federally funded research on dietary supplements.
- Collaboration with other federal agencies to develop a coordinated approach to assessment of the health effects of bioactive factors in food and dietary supplements.
- Publishing Fact Sheets on dietary supplements for consumers.

Another component of ODP, the ORD, was formally established through the Rare Diseases Act of 2002, Public Law 107–280. The budget request for fiscal year 2007 for ORD is \$15,548,000, the same amount as the fiscal year 2006 level. The following are highlights of ORD activities: (1) An Extramural Rare Diseases Clinical Research Network that involves 10 consortia with 70 sites, and 30 patient support organizations for almost 50 rare diseases. Twenty-two clinical protocols have been approved and another 25 will be developed during 2006. (2) ORD provides support for 20 Bench-to-Bedside research projects in the NIH Intramural Research Program and supports collaborative research efforts with the National Human Genome Research Institute. (3) ORD also co-funds with the NIH institutes and centers approximately 80 to 100 scientific conferences per year to identify scientific opportunities or stimulate research where it is lagging or lacking. (4) To assist the rare diseases research community and patients with rare diseases, ORD initiated a pilot program to develop genetic tests from gene discoveries in the research laboratories to the clinic. (5) ORD is developing a Web-based database of rare diseases bio-specimen repositories in the United States to facilitate access to human biomaterials for research.

OFFICE OF SCIENCE EDUCATION

The Office of Science Education (OSE), within the Office of Science Policy, develops science education programs to enhance efforts to attract young people to biomedical and behavioral science careers and to improve science literacy in both adults and children. The OSE creates programs to improve science education in schools (the NIH Curriculum Supplement Series); creates programs that stimulate interest in health and medical science careers (LifeWorks Web site); creates programs to advance public understanding of medical science, research, and careers; and advises NIH leadership about science education issues. Programs target diverse populations including under-served communities, women, and minorities, with a special emphasis on the teachers of students from Kindergarten through grade 12. The OSE Web site is a central source of information about available education resources and programs, <http://science.education.nih.gov>. The fiscal year 2007 budget request for OSE is \$3,839,000, the same as the fiscal year 2006 level.

LOAN REPAYMENT AND SCHOLARSHIP PROGRAM

The NIH, through the Office of Loan Repayment and Scholarship (OLRS), administers the Loan Repayment and Undergraduate Scholarship Programs. The NIH Loan Repayment Programs (LRPs) seek to recruit and retain highly qualified physicians, dentists, and other health professionals with doctoral-level degrees to biomedical and behavioral research careers by countering the growing economic disincentives to embark on such careers, using as an incentive the repayment of educational loans. There are loan repayment programs designed to attract individuals to clinical research, pediatric research, health disparities research, and contraception and infertility research, and to attract individuals from disadvantaged backgrounds into clinical research. The AIDS, intramural Clinical, and General Research Loan Repayment Programs are designed to attract investigators and physicians to the NIH's intramural research and research training programs. The NIH Undergraduate Scholarship Program (UGSP) is a scholarship program designed to support and enhance the training of undergraduate students from disadvantaged backgrounds in biomedical research careers and employment at the NIH. For fiscal year 2006, the UGSP plans to award scholarships and provide funding for summer internship service pay-back for twenty (20) individuals and provide funding for twenty-one (21) individuals performing one-year service payback at a cost of \$768,000. In fiscal year 2006, the Loan Repayment Program for Research Generally (GR-LRP) plans to award contracts to fifty-one (51) individuals entering into initial three-years contracts, and forty (40) contracts to individuals entering into one-year renewal contracts at a cost of \$5,286,000. Lastly, the NIH Clinical Research Loan Repayment Program for Individuals from Disadvantaged Backgrounds (CR-LRP) plans to award contracts to two (2) individuals entering into initial two-year contracts, and ten (10) contracts to individuals entering into one-year renewal contracts at a cost of \$483,000 in fiscal year 2006. The fiscal year 2007 budget request for OLRS is \$7,141,000, the same as the fiscal year 2006 level.

OFFICE OF PORTFOLIO ANALYSIS AND STRATEGIC INITIATIVES

In fiscal year 2005, the NIH established a new office within the Office of the Director, the Office of Portfolio Analysis and Strategic Initiatives (OPASI). The OPASI is made up of three divisions, focused on (1) resource development and analysis (including the development and deployment of knowledge management; (2) strategic coordination; and (3) evaluation and systematic assessments. Collectively, these three divisions identify and integrate information to support the planning and implementation of trans-NIH initiatives that address exceptional scientific opportunities and emerging public health needs. More specifically, OPASI is facilitating a "functional integration" of strategic planning and evaluation activities across the agency. The fiscal year 2007 budget request for OPASI is \$3,000,000, an increase of \$1,020,000 over the fiscal year 2006 level.

When fully staffed by fiscal year 2008, OPASI will have approximately 72 FTEs. Thirteen existing FTEs transferred to OPASI in fiscal year 2006, and approximately 16 FTEs will be recruited during fiscal year 2006. The NIH is in the process of recruiting for a Director, OPASI and expects to fill this position in 2006. Funding for fiscal year 2007 will cover additional recruitments and Office operations in an amount consistent with OPASI's structure and responsibilities. In addition to salaries to support the FTEs, funding will be used to pay for contractual services, supplies, equipment, office rent and other services.

Through these efforts, the NIH Director and the IC Directors will have access to more consistent information to improve coordination and facilitate collaboration across the agency, and to inform priority setting and budget decisions. The governance process for OPASI will likely be carried out by a new working group of the NIH Steering Committee, as described above. The group will be charged with monitoring the overall effectiveness of the office, advising on policy and planning issues, and forecasting the need for changes in OPASI's activities, among other areas.

Thank you, Mr. Chairman for giving me the opportunity to present this statement; I will be pleased to answer questions that the Committee may have.

 PREPARED STATEMENT OF DR. STORY C. LANDIS, DIRECTOR, NATIONAL INSTITUTE OF NEUROLOGICAL DISORDERS AND STROKE

Mr. Chairman and Members of the Committee, I am Story Landis, Director of the National Institute of Neurological Disorders and Stroke (NINDS). I am pleased to present the fiscal year 2007 President's budget request for NINDS.

The mission of the NINDS is to reduce the burden of neurological disorders by developing ways to prevent or to treat these diseases. Epilepsy, autism, cerebral palsy, muscular dystrophy, spinal muscular atrophy (SMA), and hundreds of other disorders are first evident in infancy or childhood. Multiple sclerosis, spinal cord injury, migraine, and traumatic brain injury are among the many nervous system diseases that are prevalent in young adults. Stroke, dementias, chronic pain, and Parkinson's disease will increase, if unchecked, with the aging of our population. The impact of neurological disorders on people, on their families, and on our economy is immense.

CLINICAL RESEARCH

The NINDS currently supports more than 1,000 clinical research projects, of which more than 125 are clinical trials of interventions to prevent or treat disease. Ongoing clinical trials are testing drugs, natural biological molecules, surgery, deep brain stimulation, hypothermia, radiation, immunotherapy, and behavioral therapies for disorders including amyotrophic lateral sclerosis (ALS), brain tumor, cerebral palsy, epilepsy, headache, Huntington's disease, multiple sclerosis, muscular dystrophy, myasthenia gravis, pain, Parkinson's disease, spinal muscular atrophy, stroke, Tourette syndrome, and traumatic brain injury.

Last year an NINDS clinical trial showed that aspirin prevents stroke effectively for the many people with partially blocked arteries in the brain who have had a previous stroke or TIA (mini stroke). Aspirin works as well as warfarin, a drug that requires monthly monitoring and carries the risk of major hemorrhage and heart attack. This trial is another step in a long march of advances that guide physicians in preventing stroke in particular risk groups. The U.S. Centers for Disease Control and Prevention estimated that the death rate from stroke declined by 18.5 percent for the U.S. population from 1993 to 2003, and progress is continuing with results like these.

Each year also brings results from several NINDS preliminary clinical trials. Current drugs for Parkinson's disease ultimately fail because they do not halt the progressive death of brain cells that causes this disease. The Neuroprotection Exploratory Trials in Parkinson's Disease (NET-PD) is a network of 50 clinical centers throughout the United States that efficiently tests drugs to slow the underlying disease. NET-PD has completed phase II trials of four drugs that had been rigorously selected for testing from candidates suggested by scientists around the world, and just published the results of the first two. NET-PD will move quickly to a large, definitive clinical trial to test the safety and effectiveness of at least one of these drugs in preventing Parkinson's disease.

In addition to clinical trials, other types of clinical studies lead to new treatment or prevention strategies. An epidemiological study this year found that men who exercised vigorously as young adults had a 50 percent lower risk of developing Parkinson's disease in later life than men who had low levels of physical activity. Other studies determined how to predict which patients with glioblastoma, a common and deadly brain tumor, will respond to a new class of anti-cancer drugs, and discovered why infant seizures do not respond to drugs that are effective in adults and what other drugs might work better.

The NINDS Clinical Research Collaboration (CRC), now under development, will extend the reach of clinical research into more communities across the United States. The CRC engages community practice and academic neurologists to speed clinical studies; minimize costs; make clinical trials more accessible to diverse participants; facilitate trials of rare diseases; and improve transfer of research results to clinical practice in the community. Complementing the CRC, the NINDS is building a network to develop emergency treatments for neurological disorders. Stroke, seizures, traumatic brain and spinal cord injury, and other neurological disorders account for perhaps 5 to 10 percent of all medical emergencies. This program brings together specialists in emergency medicine, neurological disease and clinical trials.

GENES AND NEUROLOGICAL DISORDERS

In December, the journal *Science* chose the discovery of a gene defect that can cause Tourette syndrome as one of the 10 most important scientific advances of the year. Since the NIH budget doubling began, scientists have identified more than 100 genes associated with neurological diseases including ALS, ataxias, Batten disease, dyslexia, dystonia, epilepsy, muscular dystrophies, Parkinson's disease, peripheral nerve diseases, and spinal muscular atrophies.

Gene discoveries often have a rapid impact on patients and families. They yield definitive DNA diagnostic tests that are faster, cheaper, and more accurate, and allow genetic counseling and attention to special risks of people with particular in-

herited disorders. For example, patients with ataxia used to undergo MRI brain scans, withdrawal of spinal fluid for analysis, tests for amino acids and organic acids, lipoprotein electrophoresis, urine heavy metal screens, thyroid function tests, and sometimes painful nerve or muscle biopsies to get a diagnosis, costing thousands of dollars over several months. Today, a commercially available DNA test can often give a definitive diagnosis of a genetic neurological disorder within a week for a few hundred dollars.

Gene findings also jumpstart therapy development. Over the last year, studies of therapies in animal models, another benefit from gene discoveries, have shown promise for neurofibromatosis, muscular dystrophy, Fragile X syndrome, Huntington's disease, hereditary ataxias, and several other disorders. Therapies are already moving from animal models into NIH or private sector clinical trials, including ceftriaxone for ALS, anti-oxidants for ataxia-telangiectasia, myostatin inhibitors and gentamicin for muscular dystrophy, and coenzyme Q10 for Huntington's disease. The pace is remarkable after decades without progress for many of these diseases.

Knowing where and when genes are active is key to understanding the nervous system in health and disease. Most genes are active at some time and place in the brain, yet only a small fraction of these have been well characterized, so the NINDS initiated the GENSAT (Gene Expression Nervous System Atlas) to map gene activity in the brain across development. GENSAT also generates valuable research tools including strains of mice in which a visible marker is turned on where and when the gene of interest is active. Using these mice, scientists this year found new insights into Parkinson's disease that could not have been revealed without this resource. The studies showed that one of two previously undistinguishable types of nerve cells is selectively affected in Parkinson's disease, helped explain why brain movement control circuits malfunction, revealed the molecular mechanism that kills those cells, and identified a potential new target for drugs to slow Parkinson's disease.

TRANSLATIONAL RESEARCH

With the budget increases, the NINDS implemented major programs to move insights from basic research to practical therapies ready for testing in clinical trials, that is, translational research. The Cooperative Program for Translational Research supports research teams in academia and small companies. These milestone-driven, investigator-initiated projects are developing drug, stem cell, or gene therapies for Batten disease, Parkinson's disease, Huntington's disease, tuberous sclerosis, Duchenne muscular dystrophy, traumatic brain injury, and stroke, among other disorders.

In another translational effort, the NINDS developed the SMA Project as a model program to expedite therapy development. The contract-based project is making encouraging progress towards its ambitious goal—having a drug for SMA ready for clinical trials by the end of 2007. A steering committee, with drug development expertise from industry, the FDA, academia, and the NIH, first developed a detailed drug development plan. To carry out the plan, the project then created a virtual drug development company with the tools and facilities for identifying “lead compounds,” chemically modifying leads into potentially improved compounds, testing drug candidates in cell and animal models, and coordinating the overall drug development scheme. More than 300 compounds have been prepared and are in testing. In 2007, the NINDS will address a major barrier in the development of drugs for other neurological diseases by extending the contract-based medicinal chemistry resource from the SMA Project. Medicinal chemists modify weakly active compounds so that drug development teams can test the new drugs for improved safety and effectiveness.

NIH basic science stimulates therapy development in the private sector, as well as by the NIH. In the past year, private sector clinical studies of clotting Factors VII and VIIa have shown promise for serious and hard to treat strokes caused by bleeding in the brain. NIH research motivated those studies by showing that these strokes are followed by continued expansion of blood filled pockets in the brain, called hematomas, which contribute profoundly to disability and death. Private sector clinical trials in gene and cell therapies for Parkinson's disease begun this year also build upon NINDS research.

Longstanding NINDS targeted therapy development programs also catalyze private sector efforts. For three decades, the Anticonvulsant Screening Program (ASP) has fostered industry development of drugs for epilepsy, including six drugs in widespread use and several more now in clinical testing. Drugs that emerged from the ASP testing program are also among the most effective treatments for chronic pain. NINDS initiatives begun last year and to begin in 2007 focus on animal models for

testing drugs that block the development of epilepsy, work for treatment resistant epilepsy, and meet the special needs of pediatric and geriatric populations.

COLLABORATIVE RESEARCH

The NINDS strongly encourages cooperative efforts among scientists and physicians from diverse disciplines, and works closely with other parts of the NIH, other government agencies, and non-governmental organizations, as well as with companies. As may be evident from the discussions of the Clinical Research Consortium, NET-PD, GENSAT, the Cooperative Program in Translational Research, and the SMA Project, most NINDS programs, whether focused on a particular disease or a scientific problem, emphasize collaboration. Other examples include research centers on muscular dystrophy, Parkinson's, autism, spinal cord injury, stroke and health disparities, and resources including the Human Genetics Repository and the Microarray Consortium.

The NIH Neurosciences Blueprint, begun in 2005, presents a framework to enhance cooperation across the NIH institutes that share an interest in diseases of the nervous system. Blueprint initiatives have focused on neuroscience tools, training in the neurobiology of disease for basic scientists, genome analysis, neuroimaging, genetic mouse models, core research facilities, and clinical assessment tools. In 2007, the Blueprint will focus on neurodegeneration, which contributes to many diseases.

Among government agencies, the NINDS is working closely with the U.S. Army Medical Research Institute of Chemical Defense (USAMRICD) because many potential chemical terrorist agents affect the nervous system. Cooperative projects with the Veterans Administration include a major clinical trial of deep brain stimulation for Parkinson's disease. The NINDS also meets regularly with the FDA on stem cells and other biological therapies and works with the National Science Foundation on common interests including computational neuroscience and informatics.

More than 300 non-governmental organizations (NGOs) focus on diseases within the mission of the NINDS. The World Parkinson Conference, held for the first time this February, and a major conference on epilepsy planned for March 2007 are two of many recent examples of cooperative efforts between NGOs and the NINDS. In June 2005, the Institute brought together 75 representatives of NGOs at the NIH for a day of presentations, informal interaction, and group discussions. Based on the strong positive feedback from participants, the NINDS will hold similar meetings in the future to explore how we can work together in the future.

Thank you, Mr. Chairman. I would be pleased answer questions from the Committee.

PREPARED STATEMENT OF DR. TING-KAI LI, DIRECTOR, NATIONAL INSTITUTE ON ALCOHOL ABUSE AND ALCOHOLISM

Mr. Chairman and members of the Committee: I am pleased to present the fiscal year 2007 President's budget request for the National Institute on Alcohol Abuse and Alcoholism (NIAAA). The fiscal year 2007 budget includes \$433,318,000, which reflects a decrease of \$2,612,000 over the fiscal year 2006 enacted level of \$435,930,000 comparable for transfers proposed in the President's request.

Alcohol consumption kills or disables thousands of Americans each year. The Centers for Disease Control and Prevention (CDC) reported in 2005 that, in the mid-1990s, alcohol use and abuse were among the top ten causes of death and disability in the United States. CDC also ranked excessive alcohol consumption as the third leading preventable cause of death in 2001. Motor vehicle crashes are among the most visible consequences of alcohol use; CDC estimates that in 2003, 40 percent of traffic deaths were alcohol-related. However, death and disability also result from alcohol-related diseases, such as liver cirrhosis, heart disease, stroke, dementia, and certain cancers.

Despite these consequences, the majority of people who drink are able to do so without harm to themselves or others. One of the fundamental goals of alcohol research is to determine why some individuals cannot limit their drinking. Research has shown clearly that half of the risk for developing alcohol use disorders is a function of genes, while the other half can be traced to factors in the environment, such as family, friends, and culture. The measure of risk is not an either/or situation; genes and environmental factors interact and influence one another, even at the molecular level.

Investigating the interplay of genes and environment is an important focus across the NIH, with implications for many of the most widespread, life-threatening, and costly health conditions affecting Americans. One of the exciting areas of research I would like to describe today has to do with how new tools we are developing to

investigate this interaction between genes and environment can contribute to an understanding of alcohol dependence.

As a starting point, we have already identified several genes that can raise or lower the risk of developing alcohol dependence. Variants in two families of genes that are involved directly in alcohol metabolism, for example, can lower risk. These genes encode enzymes that break down alcohol. Some people inherit enzyme variants that will result, if a person drinks, in especially high levels of a toxic by-product of alcohol metabolism. These individuals feel sick when they drink; as a result, they are at lower risk of developing alcohol use disorders.

Other genes that play a role in alcoholism risk encode the communication circuitry of brain messenger molecules, the receptors of neurotransmitters, a number of which have been linked to alcoholism and psychiatric disorders that co-occur frequently with alcoholism. Research suggests, for example, that genes for neurotransmitters involved in depression and anxiety are also, in some groups, related to alcoholism risk. Among the neurotransmitter systems for which research has reported a relationship between genes and alcoholism risk: GABA, a neurotransmitter that slows the pace of brain signaling and is known to be involved in the alcohol response; NPY, a brain protein involved in stress responses and memory; serotonin, a neurotransmitter involved in the regulation of mood; and brain opioids, which play a role in the sensation of pleasure.

Variants in these neurotransmitter genes influence alcoholism risk by shaping how the brain responds to alcohol, regulating how pleasant the experience is, or how sedating. An important new direction of research has to do with investigating how the opposite can occur: alcohol can make lasting changes in genes in ways that can have profound effects on health.

Epigenetics refers to heritable and long-term changes in gene function that occur without a change in DNA sequence. Such changes could be caused, for example, by elements in the environment, such as alcohol, changing how genes are translated into proteins, in other words, how the genes are expressed. Epigenetics can help us understand how alcohol has lasting effects on health.

One of the ways alcohol and its metabolites can change gene expression is by modifying histones—proteins that intertwine with DNA. Stable modification of DNA can also occur. Both of these reactions can activate or silence the expression of genes. Alcohol through its metabolism contributes to or alters the level of at least two specific metabolites that are required for these chemical modifications.

Epigenetic modifications may be transmitted as the cell divides. Thus, these modifications may persist throughout the lifespan. Epigenetic changes also have the potential to be passed on to the next generation, producing abnormalities in offspring. This research, at the forefront of progress in genetics and molecular biology, gives us an opportunity to understand the complex mechanisms by which an external environmental factor like alcohol interacts with biology. It promises to help explain why repeated exposure to alcohol can change permanently how a person responds thereafter to the substance, setting the stage for dependence. It can help explain why drinking during pregnancy can cause irreversible damage to the brain of a fetus. And it may help explain what underlies alcohol's destructive effects on such organs as the liver, pancreas, and brain, as well as its role in cancers associated with heavy alcohol exposure.

Epigenetics research may also provide a means for investigating the long-term effects of alcohol consumption on adolescents. Alcohol is the drug most commonly used by youth. Adolescents who drink tend to do so intensively; according to 2005 data from the Monitoring the Future study, 11 percent of 8th graders, 21 percent of 10th graders, and 28 percent of 12th graders report drinking 5 or more drinks in a row in the past two weeks. This "binge" drinking is a particularly hazardous pattern of drinking at any age. But during adolescence, when the brain is still undergoing developmental change, binge drinking may have particular dangers.

Preliminary studies suggest that alcohol has the potential to disturb normal brain development in adolescence and young adulthood. NIAAA research has established that youth who begin to drink in their early teens are at greater risk later of developing alcohol dependence. This increased risk can be explained only partly by inherited biological risk factors, suggesting that early drinking itself causes changes that manifest themselves in future behavior. Data from NIAAA's National Epidemiologic Survey on Alcohol and Related Conditions has shown that most cases of alcoholism are established by age 25. This suggests that alcoholism, rather than being a disease of middle age, is a developmental disorder that has its roots in youth.

An important NIAAA initiative is aimed at investigating the effects of alcohol, including epigenetic effects, on developing brain structures and systems that regulate behavior. It will address the mechanisms that underlie alcohol-related changes during brain development, the dosage and drinking patterns that result in changes, and

the factors that promote or protect against these changes. An important aim of this research is to determine whether and how alterations in brain function influence lifetime risk for alcohol use disorders, particularly in vulnerable individuals.

Improving our fundamental understanding of how the environment interacts with genes has many potential benefits. For example, knowledge of the genes that are related to risk for alcohol problems—and how variants of these genes might be manifest in physical or behavioral traits—can be used to assist in the identification of individuals at risk or, in other words, predict who is vulnerable. Understanding how alcohol interacts with genes will help define how an individual makes the transition from casual drinking to dependence; and how long term heavy drinking causes disease.

Our growing body of knowledge about genes and the cellular processes they encode is providing targets for medications development. Genetics research is helping to show why no one medication will work in every person. The ultimate goal will be to personalize treatment—similar to the approach in diseases like hypertension or depression—by choosing from an array of medications the agent that is most effective for a given individual.

Finally, among its most important potential benefits, the investigation of genes and environment will give us a clear picture of the impact of alcohol on the long-term health and behavior of adolescents. Understanding the mechanisms behind these persistent effects will make even more compelling the imperative to identify effective ways of preventing adolescents from consuming alcohol, not only to safeguard their health and well-being in youth, but to preempt the development of alcohol use problems in adulthood.

Thank you Mr. Chairman. I would be pleased to answer any questions that the Committee may have.

PREPARED STATEMENT OF DR. DONALD A.B. LINDBERG, DIRECTOR, NATIONAL
LIBRARY OF MEDICINE

Mr. Chairman and Members of the Committee: I am pleased to present the President's budget request for the National Library of Medicine (NLM) for fiscal year 2007, a sum of \$313,269,000, which is \$1,641,623 less than the comparable fiscal year 2006 appropriation.

Only a few years ago we frequently described the role of the National Library of Medicine almost entirely in the context of the medical literature—NLM collected and organized the books and journals that were then used in the process of making new discoveries that would be reported in yet more books and journals. That paradigm, although accurate as far as it goes, is no longer sufficient to describe the Library's role. Today, the NLM is at the hub of an interconnected world of an amazing amount of information, ranging from the published literature, to molecular sequence and genomic data, to descriptions of clinical trials, to still and moving medical images, to maps of chemical spills and other information used for emergency preparedness, and to authoritative research-based information prepared especially for the general public—for patients and their families and caregivers.

The range of persons and institutions with which the Library interacts is staggering. A National Network of Libraries of Medicine, with more than five thousand members, extends the reach of NLM's services. Many medical organizations, publishers, academic institutions, government agencies, and libraries make data available to the world through the National Library of Medicine. The NLM, with a staff of experienced medical librarians, scientists, and health professionals, creates databases and other Web resources to ensure that high quality information is available to all, easily and without restriction. The bottom line of all this is that the Library operates the most-consulted scientific medical Web site in the world: two million people come to the Library's Web site—to learn about diseases, search the literature, connect with other information providers, and to download terabytes of data—every day.

As a key member of the NIH research team, the Library works closely with scientists on the Bethesda campus and around the country. A prime example of this is the work of NLM's National Center for Biotechnology Information (NCBI) and the panoply of databases with genomic information contributed by NIH and NIH-supported scientists. This collaboration extends around the world, with partners at institutions in other nations contributing sequence and other data to the NCBI's databases. Another example of extensive collaboration is that several thousand public and private organizations have agreements with NLM to use the Visible Human Project datasets of anatomical information to create techniques and software used in teaching and research.

But the Library is also a bricks and mortar facility on the campus of the National Institutes of Health. NLM has two reading rooms that are open to the public—one that serves the Library's remarkable collection of historical materials and a main reading room. An exhibition, "Visible Proofs: Forensic Views of the Body," has just been opened in the Library's public area and will be visited by many thousands, including students from grade school up. Previous exhibitions are now touring the country, extending greatly the work of our history of medicine curators.

A basic function of the National Library of Medicine is to serve as a "court of last resort" for seekers of medical information. With the world's largest collection—eight million items—the NLM is relied on by institutions and individuals around the globe.

INFORMATION SERVICES FOR THE PUBLIC

The Library's main portal for consumer health information is MedlinePlus, available in both English and Spanish. Much of this material is based on research done or sponsored by the NIH Institutes. MedlinePlus has more than 700 "health topics," containing, for example, overview information, pertinent clinical trials, alternative medicine, prevention, management, therapies, current research, and the latest news from the print media. In addition to the health topics, there are medical dictionaries, a medical encyclopedia, directories of hospitals and providers, and interactive "tutorials" with images and sound. The newest addition to MedlinePlus is a series of surgical videos that show actual operations of common surgical procedures. Another new aspect of MedlinePlus is "Go Local," that is, a service to link users from the MedlinePlus health topics to the health and social services in their community that are related to that topic.

There are other popular NLM Web sites for the public. ClinicalTrials.gov was created to give everyone easy access to information about human research studies. The site contains information on more than 25,000 federally and privately supported trials. It includes summaries of the purpose of each study, the recruiting status, criteria for patient participation, location(s) of the trial and specific contact information. NIHSeniorHealth.gov is maintained by the Library in collaboration with the National Institute on Aging and other NIH Institutes. At present there are 22 topics of interest to seniors, including, for example, Alzheimer's Disease, balance problems, macular degeneration, shingles, and stroke. NIHSeniorHealth.gov contains information in a format that is especially usable by seniors, with, for example, large type, and it also has a "talking" function that allows users to listen as the text is read to them.

NLM's Genetics Home Reference provides consumer-friendly summaries of genetic conditions and related genes and chromosomes. This information resource bridges consumer health information and scientific bioinformatics data, and it links to many existing resources, both at NLM and at other reliable sites. The Household Products Database provides easy-to-understand data in consumer-friendly language on the potential health effects of more than 2,000 ingredients contained in more than 6,000 common household products. The Household Products Database has proved to be popular with the media, and there have been a number of newspaper and magazine articles about it. Another consumer health site is the colorful Tox Town, which looks at an ordinary town and points out many harmful substances and environmental hazards that might exist there. Users can click on a town location, like a school, office, factory, or park and find information about the toxic chemicals that may be encountered there. Other versions are available for a big city, a farm, and the U.S.-Mexico border area. There is also a new special section with information on toxic chemicals and disaster health concerns in the wake of Hurricane Katrina and Hurricane Rita.

INFORMATION SERVICES FOR THE SCIENTIFIC COMMUNITY

The most frequently consulted online medical resource in the world is PubMed/Medline, an easily searchable database of more than 15 million references and abstracts for medical journal articles from the 1950s to the present. Usage of PubMed/Medline by the scientific and lay communities has grown considerably since it became free on the Web in 1997, to over two million searches per day. PubMed also links to the sites of participating publishers so that users can retrieve full-text articles from 5,000 journals. Where links to electronic full text are not available, the user may use PubMed to place an online order for an article directly from a library in the National Network of Libraries of Medicine.

PubMedCentral (PMC) is a Web-based repository of biomedical journal literature providing free and unrestricted access to the full-text of articles. This repository is based on a natural integration with the existing PubMed/Medline biomedical lit-

erature database of references and abstracts. Currently, PMC contains nearly 600,000 full-text articles. Recent additions have come from newly published material as well as from digitizing back issues that previously were only available in printed form. NIH's Public Access policy encourages scientists whose work is funded by the NIH to submit their manuscripts to PubMed Central. NLM's National Center for Biotechnology Information designed and implemented the NIH Manuscript Submission system, a quick and easy-to-use system for scientists to submit their manuscripts. Creating such digital archives as PubMedCentral to ensure that the world's biomedical literature is properly recorded and available for future generations, is an important NLM responsibility.

Another heavily used scientific resource is a database of all publicly available DNA sequences, called GenBank. The NCBI, which maintains GenBank, has also created integrated retrieval tools that allow seamless searching of the sequence data and provide links to related sequences, bibliographic citations, and other resources. Such features allow GenBank to serve as a critical research tool in the analysis and discovery of gene function as well as discoveries that lead to identification and cures for a number of diseases. One recent example of the use of NCBI sequence databases was to identify the first polio case in the United States since 1999. The state health laboratory in Minnesota had isolated an unknown virus from a hospitalized child from an Amish community. The laboratory staff went to the Web, searched against the 55 million DNA sequences at NCBI, and found a match to the polio virus used in the Sabin oral vaccine. "Bingo," said the laboratory's director, "It was a 98 percent match. We knew we had nailed it."

A critical need in biomedical research, as identified in the NIH Roadmap Initiative, is a repository for what are called "small molecules" that are crucial in drug development. Small molecules are responsible for the most basic chemical processes that are essential for life and they often play an essential role in the attack of a pathogen, or in the cell's response to the attack. The new PubChem database, developed by the NCBI, links the small molecules to their biological functions and to the macromolecules with which they interact. At present, PubChem includes over 7.5 million records for small molecules with over 5 million molecular structures. These data have been contributed by public, academic, and commercial resources.

The NCBI is also doing important work on other issues of current public concern. One of these is to provide an Influenza Virus Resource that links researchers working on vaccines to genomic data about the influenza virus. As the data accumulate and the analyses progress, the discoveries made will ultimately lead to better prediction of large-scale outbreaks, more effective vaccine design, and the saving of many human lives. Another area of NCBI work of topical interest is their development, in the aftermath of 9/11, of sophisticated software called OSIRIS. The software is now being tested within five collaborating forensic DNA laboratories to assist in the analysis and validation of forensic data and help identify victims from the Gulf Coast states in the aftermath of Katrina.

A recently announced series of initiatives by several NIH Institutes directed at understanding the genetic factors underlying human disease will require the NCBI to play a key role. Several large-scale, long-term studies, such as the Framingham Heart Study, will be adding genetic information from participants to the clinical data already collected. NCBI has been selected by the Institutes to build the databases that will incorporate the clinical and genetic data, link them to the molecular and bibliographic resources at the NCBI and, for the first time, make these data available to the scientific and clinical research community.

NLM remains the principal source of support nationally for research training in the field of biomedical informatics. This support is especially important as rapidly moving technology in health care and biomedical research requires investigators who understand biomedicine as well as fundamental problems of knowledge representation, decision support, and human-computer interface. Five-year institutional training grants from NLM support some 300 pre-doctoral, post-doctoral, and short-term trainees across the country.

OTHER AREAS OF INTEREST

The Library has an important role in developing standards for Electronic Health Records. As part of its Unified Medical Language System (UMLS) project, NLM creates vocabulary databases and software tools to assist informatics researchers and system developers in automated interpretation and integration of medical knowledge and health data. Chief among the UMLS resources is the Metathesaurus, which links and provides 4.7 million concept names for 1.2 million concepts from 114 vocabularies in a single database format. The UMLS serves as a common distribution vehicle for standard code sets and vocabularies needed for administrative

transactions and electronic health records, as well as a resource for advanced natural language processing, automated indexing, and enhanced information retrieval. Building on its two decades of UMLS experience, the Library also serves as an HHS coordinating center for standard clinical vocabularies, such as the SNOMED CT clinical terminology. The Library works closely with the Office of the National Coordinator for Health Information Technology and other organizations to align health data standards into an effective interlocking set and to promote more rapid adoption of standards-based electronic health records to facilitate patient care, public health surveillance, and clinical research.

Twenty years ago the National Library of Medicine published a long range plan that has proved to be of enormous benefit to the institution. Out of it grew such initiatives as the Visible Human Project, the National Center for Biotechnology Information, and the recommendation that the Library engage in an outreach campaign to reach minority and other underserved health professionals. The Library is now engaged in a similar planning exercise for the next decade. Leaders from across the spectrum of health and medicine are meeting at the Library to consider four major themes relating to resources and infrastructure, outreach to the underserved, support for clinical and public health systems, and support for genomics. The plan, which will be issued by the NLM Board of Regents and published later in 2006, will point the Library in the direction in which it can make its maximum contribution to society.

PREPARED STATEMENT OF JUANITA M. MILDENBERG, ACTING DIRECTOR, OFFICE OF
RESEARCH FACILITIES DEVELOPMENT AND OPERATIONS

Mr. Chairman and Members of the Committee: I am pleased to present the President's budget request for the Buildings and Facilities (B&F) Program for fiscal year 2007, a sum of \$81,081,000.

ROLE IN THE RESEARCH MISSION

State-of-the-art facilities for scientific research and research support facilities are a vital part of the research enterprise. The National Institutes of Health's (NIH) Buildings and Facilities (B&F) program designs, constructs, repairs and improves the agency's portfolio of laboratory, clinical, animal, administrative and support facilities at its six installations in four states. These facilities house researchers from the NIH Institutes' and Centers' (ICs) intramural basic, translational, and clinical research programs; science administrators who oversee NIH's grants; the NIH leadership, and various programs that support agency operations. The fiscal year 2007 B&F budget request focuses on the need for responsible utilization and stewardship of NIH's past and recent investments in the "bricks and mortar" of the research enterprise. In order to stay abreast of the changing needs of the NIH programs, it is imperative that we provide reliable, safe and secure research support facilities that are appropriately equipped, operated and maintained.

The B&F budget request is the product of a comprehensive, corporate capital facilities planning process. This process begins with extensive consultation across the research community and the NIH's professional facilities staff. It works through the Facilities Working Group, an advisory committee to the NIH Steering Committee, and the HHS Capital Investment Review Board. Through this process, the program demand for more effective and efficient facilities designed to support current and emerging investigative techniques, technologies, and tools is integrated with, and balanced against, the need to repair, renovate, and improve the existing building stock to keep it in service and to optimize its utility.

The fiscal year 2007 request provides the necessary funding support for the ongoing safety, renovation and repair, and related projects that are vital to proper stewardship of the entire portfolio.

The fiscal year 2007 B&F budget request is organized among three broad Program Activities: Essential Safety and Regulatory Compliance, Repairs and Improvements and Construction. The fiscal year 2007 request provides funds for specific projects in each of the program areas. The projects and programs enumerated are the end result of the aforementioned NIH facilities planning process and are the NIH's capital facility priorities for fiscal year 2007.

FISCAL YEAR 2007 BUDGET SUMMARY

The fiscal year 2007 budget request for Buildings and Facilities is \$81.1 million. The B&F request contains a total of \$14.5 million for Essential Safety and Regulatory Compliance programs composed of \$2 million for the phased removal of asbes-

tos from NIH buildings; \$5 million for the continuing upgrade of fire and life safety deficiencies of NIH buildings; \$1.5 million to systematically remove existing barriers to persons with disabilities from the interior of NIH buildings; \$1 million to allow for environmental remediation activities at NIH sites; and \$5 million for the continued support of the rehabilitation of animal research facilities. In addition, the fiscal year 2007 request includes \$65.9 million in Repairs and Improvements for the continuing program of repairs, improvements, and maintenance that is the vital means of maintaining the complex research facilities infrastructure of the NIH; and \$700,000 in Construction for pre-project planning including concept development studies and analyses of NIH-wide facility projects proposed in the facilities plan.

My colleagues and I will be happy to respond to any questions you may have.

PREPARED STATEMENT OF DR. RODERIC I. PETTIGREW, DIRECTOR, NATIONAL
INSTITUTE OF BIOMEDICAL IMAGING AND BIOENGINEERING

Mr. Chairman and Members of the Committee: I am pleased to present the fiscal year 2007 President's budget request for the National Institute of Biomedical Imaging and Bioengineering (NIBIB). The fiscal year 2007 budget includes \$294,850,000; a decrease of \$1,960,000 over the fiscal year 2006 enacted level of \$296,810,000 comparable for transfers proposed in the President's request.

BRIDGING THE PHYSICAL AND LIFE SCIENCES

The mission of the NIBIB is to improve human health by leading the development and accelerating the application of biomedical technologies. The Institute is committed to integrating the engineering and physical sciences with the life sciences to advance basic research and medical care. To demonstrate our commitment, the NIBIB gives special consideration for funding to research grant applications that bridge and integrate the life and physical sciences.

TRANSLATING TECHNOLOGY INTO CLINICAL PRACTICE

Ultimately, the NIBIB seeks to translate research findings made in the laboratory into solutions that advance human health by reducing disease burden and improving quality of life. One highly successful example of a research and commercialization effort supported in part by the NIBIB is an automated, digital-imaging device called the "array microscope." The system utilizes an array of 100 miniaturized objectives to produce a single, seamless sweep of a microscope slide of a histopathology sample. The result is a microscopic-level resolution, multi-colored digitized image of the pathology sample. The most immediate impact of this technology is expected to be in medical pathology. These "virtual slides" can be easily stored in a patient's record and can also be viewed over the Internet, providing immediate on-line access to expert second opinions.

The recently released "Quantum Project" initiative is another example of how the NIBIB strives to support a more integrated and focused research agenda using multidisciplinary approaches to develop innovative and marketable technologies. The goal of this unique program is to make a "quantum" advance in healthcare by funding research on a specific project or projects that will translate into new technologies and modalities for the treatment, prevention and cure of disease or resolve a major health care problem within a reasonable time frame. In these "bench to bedside" partnerships, a team of interdisciplinary scientists will conduct collaborative research that will result in a prototype product that can be translated into clinical practice.

TECHNOLOGIES TO IMPROVE HEALTH CARE DELIVERY

With the advent of miniaturized devices and wireless communication, the way in which doctors care for patients has changed dramatically. Empowering clinicians to make decisions at the bedside, or the "point-of-care," has the potential to significantly impact health care delivery and help address the challenges of health disparities. The success of such a shift relies on the development of portable diagnostic and monitoring devices for near-patient testing. The NIBIB has contributed to advances in this area by funding the development of sensor and microsystem technologies for point-of-care testing. These instruments combine multiple analytical functions into self-contained, portable devices that can be used by non-specialists to detect and diagnose disease, and can enable the selection and monitoring of optimal therapies. These advances limit the reliance on submission of samples to centralized laboratories and will make results more readily available within minutes as opposed to several hours or days, enabling clinicians to make decisions regarding treatment

when these decisions can have the greatest impact. An example under development at the NIBIB is a handheld system for the rapid detection and identification of bacteria which cause urinary tract infections. The research team anticipates this test could become available in the next two to three years. To further capitalize on these advances, the NIBIB is planning an initiative to support research on critical areas for the development of other hand-held, diagnostic devices. These systems could reduce the cost of health care, much as integrated electronics have reduced the cost of computing, and greatly simplify and improve patient delivery of care.

NEXT GENERATION MINIMALLY-INVASIVE TECHNOLOGIES

Advances in imaging technologies have spurred new minimally-invasive procedures to accurately identify the site of disease and injury, provide tissue for a definitive diagnosis, administer treatment with minimal trauma, and monitor treatment responses. Image-guided interventions are not only more efficient in terms of time and cost, but their less invasive nature may result in fewer complications and less damage to tissue. For example, NIBIB investigators are developing new magnetic resonance imaging (MRI) techniques to detect and treat organ rejection non-invasively. The current standard for diagnosing and staging rejection is the biopsy, which is invasive, painful, and prone to sampling errors that can yield false negative results. The development of a non-invasive imaging-based method that can replace the biopsy is highly desirable.

Over the next year, the NIBIB intends to expand its image-guided interventions program by supporting research on the development of technologies that allow the surgeon to visualize the patient seamlessly, in three-dimensional preoperative images; track intraoperative changes with real-time imaging; and restore a normal sense of touch through robotic tools with sensors for touch feedback, or haptics. This research may lead to new minimally-invasive surgical procedures with fewer complications, shorter hospital stays, and reduced costs. To plan for future initiatives in this area, the NIBIB recently organized an interagency retreat to identify high priority challenges that can serve as short- and long-term goals. Eight Federal agencies and nine NIH Institutes and Centers (ICs) participated in this retreat.

SMEDICAL ROBOTIC

First generation surgical robots are already being installed in a number of operating rooms around the country. Although these robots can't perform surgery on their own, they are certainly lending a mechanical hand. Robots are being used in medicine because they allow for unprecedented control and precision of surgical instruments and reduce trauma to the patient, dramatically improving surgical outcomes and lowering health care costs. Robots are also being used in rehabilitation as they provide considerable opportunities to improve the quality of life for physically disabled people. For example, one of the most common stroke disabilities is a paralyzed arm. The NIBIB and the National Institute of Child Health and Human Development are jointly funding the development of two robotic devices that could accelerate rehabilitation of patients with paralyzed arms and reduce the cost of physical therapy. These devices can also treat people who have experienced catastrophic events, such as war injuries resulting in limb loss. Testing with stroke patients is expected to begin this year using one device.

Traumatic injury or neurological diseases can also significantly alter or impair the lifestyle of an individual. To help patients lead more productive lives, NIBIB scientists are developing a non-invasive brain-computer interface to provide both communication and control functions. By recording brain waves from the scalp and then decoding them, this system allows people to move a cursor to spell words, and even to control a robotic arm. Initial efforts to test this new technology in the field are underway.

NANOTECHNOLOGY FOR DISEASE DETECTION AND DRUG DELIVERY

Detection of dormant metastatic tumor cells is a critical but elusive goal in cancer treatment. To find these cells, NIBIB researchers are developing non-invasive optical imaging techniques that are less costly and more accessible than MRI-based techniques and are free of the side effects associated with radioactive imaging agents. Microscopic or nanoscale "bubbles," called polymerosomes, containing embedded fluorescent materials are the key to this new approach. These labeled bubbles are injected directly into a tumor and then imaged. Also in development are polymerosomes that would deliver chemotherapy agents directly to a tumor. The surface of the bubble can carry a molecule that would bind to tumor cells, and its membrane would also hold fluorescent molecules for detection by optical imaging, with the chemotherapy "payload" carried in the interior. One investigator has developed

a special device which improves drug release by ultrasonic fragmentation of the bubble.

ENHANCED SUPPORT FOR NEW INVESTIGATORS

New investigators are the innovators of the future—they bring fresh ideas and technologies to existing biomedical research programs, and they pioneer new areas of investigation. Entry of new investigators into the ranks of independent, NIBIB-funded research is essential to the health of the biomedical imaging and bioengineering research enterprise. The NIBIB is specifically targeting new investigators for special funding consideration. This proved to be quite successful in the first year of this policy, and a continuation of this program is planned.

TRAINING FOR THE FUTURE

An important goal of the NIBIB is to train a new generation of researchers equipped to meet the modern needs of interdisciplinary and transdisciplinary research. Researchers trained in biomedical imaging and bioengineering must be able to demonstrate technical competency in multiple fields as well as the ability to think independently, communicate ideas effectively, work in teams, and contribute to a strong vision that transcends a narrow discipline. To this end, the NIBIB will work with the community to develop new programs that cross-train research scientists in the biological and quantitative sciences. For example, the NIBIB's Research Supplements to Promote Clinical Resident Research Experiences program has been very successful. This novel training mechanism is designed to serve as a "first step" in attracting outstanding clinicians into research careers related to the mission of the NIBIB by providing a one to two-year research opportunity during residency training.

The NIBIB has also developed several public and private collaborations to catalyze research at this interface. For example, the NIBIB and the Howard Hughes Medical Institute partnered in a novel public-private partnership to stimulate the development of new interdisciplinary graduate training programs that integrate the physical, quantitative, and engineering sciences with the life sciences. This program will train a new generation of researchers, equipped to meet the challenges of the 21st Century.

NIH ROADMAP FOR BIOMEDICAL RESEARCH

An overarching goal of the NIH Roadmap is to facilitate the development of broad-based innovative, novel and multidisciplinary science and technology that has the potential to further advances in health care. This goal is well aligned with the NIBIB mission and is actively supported on a number of fronts. For example, over the last year NIBIB has been the lead Institute in a Roadmap initiative entitled "Innovation in Molecular Imaging Probes." Molecular imaging approaches can be used to study cellular events and biochemical abnormalities. The major roadblocks to in vivo clinical applications of molecular imaging are the poor sensitivity and potential toxicity of the current probes. This initiative supports research programs that will circumvent these roadblocks.

NIH BLUEPRINT

The Neuroscience Blueprint is a framework designed to enhance cooperative activities among the NIH ICs that support research on the nervous system. During the last year, NIBIB contributed to the development of a number of initiatives, leading or participating in three project teams. These initiatives aim to support research and development of imaging technology for high resolution imaging of neural activity that is reflected in electrophysiological signals; and to develop a framework to address the critical need for neuroimaging data and software tools sharing and integration. The NIBIB also participated in the development of neuroscience training initiatives.

PREPARED STATEMENT OF DR. GRIFFIN P. RODGERS, ACTING DIRECTOR, NATIONAL INSTITUTE OF DIABETES AND DIGESTIVE AND KIDNEY DISEASES

Mr. Chairman and Members of the Committee: I am pleased to present the fiscal year 2007 President's budget request for the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) a sum of \$1,844,298,000, which includes \$150,000,000 for the Special Appropriation for Research on Type 1 Diabetes through Sec. 330B of the Public Health Service Act. The NIDDK transfers some of these funds to other institutes of the NIH and to the Centers for Disease Control and Pre-

vention (CDC). Adjusted for mandatory funds, this is an decrease of \$10,627,000 from the fiscal year 2006 enacted level of \$1,854,925,000 comparable for transfers proposed in the President's request.

The NIDDK supports research to combat a wide range of chronic health problems, including diabetes and other endocrine and metabolic diseases; diseases of the digestive system, kidneys, urinary tract; and blood; nutritional disorders; and obesity. Through vigorous research, initiated both by investigators and by the Institute, the NIDDK will continue to elucidate the fundamental biology underlying health and disease. We are pursuing new strategies for disease diagnosis, treatment, and ultimately, prevention and cure.

PREEMPTING CHRONIC DISEASES AND THEIR COMPLICATIONS

Chronic diseases pose some of the greatest health challenges to the Nation today. These diseases and their symptoms range in severity, but are often debilitating and sometimes fatal. Some impair fundamental body processes, such as metabolism, while others target the kidneys, liver, and other vital organs and systems. Though their causes and ultimate effects on health may differ, chronic diseases share the grim features of constant affliction and impaired quality-of-life. The burden of chronic diseases within NIDDK's research purview is immense. Recent estimates using national health survey data reveal that diabetes (type 1 and type 2) affects nearly 21 million Americans.¹ About 20 million Americans have chronically impaired kidney function, which places them at increased risk for irreversible kidney failure (end stage renal disease) and death.² Digestive diseases, such as irritable bowel syndrome (IBS), inflammatory bowel disease (IBD), and liver and biliary diseases, wreak havoc with people's lives. "Benign" diseases of the bladder and lower urinary tract, including urinary incontinence and prostate diseases, can be devastating. These chronic diseases also exact a heavy economic toll. For example, the healthcare and indirect costs of diabetes and its complications totaled \$132 billion in 2002.³ The painful, debilitating symptoms of IBS and the bladder disease interstitial cystitis (IC) result in loss of work and increased medical costs. Costs of chronic diseases that strike the digestive system, kidneys, and bladder run into the tens of billions of dollars.

The tremendous human and monetary costs of chronic disease are matched only by the extraordinary interventions often needed just to preserve life. Organ transplantation and kidney dialysis are but two examples. Although these are extreme measures for the sickest patients, they represent some of the victories achieved by biomedical research in reducing morbidity and mortality from advanced chronic disease. Our goal is to improve these treatments, while we simultaneously seek prevention strategies. For example, whole liver transplantation from deceased donors is a successful treatment for liver failure, but is limited by a shortage of donor organs. A new NIDDK clinical network (A2ALL) is maximizing this treatment option in adults by assessing the safety and outcomes, for both patients and donors, of new procedures that use partial liver transplants from living donors—thereby increasing the potential donor pool. Similarly, we are addressing the diminished quality-of-life and low five-year survival rates under current dialysis treatment, which is typically administered three times weekly. A new clinical trial will evaluate the effectiveness of daily dialysis.

IMPORTANCE OF EARLY INTERVENTION

For persons already suffering from chronic disease, improved treatments will have great benefits. However, it is imperative that researchers find ways to intervene at the earliest possible stage of a disease. The goals for such research are to: (1) identify and use biological information, such as "biomarkers," that can predict an individual's susceptibility to disease, disease progression, or disease complications—thereby enabling more tailored use of interventions; (2) find the most effective interventions to preempt the onset or course of disease; and (3) ensure that these predictive tools and interventions can be precisely targeted for the benefit of patients. New advances in science, technology, and public health research are making these goals realizable, with the prospect of significant improvements in public health. Ex-

¹National Institute of Diabetes and Digestive and Kidney Diseases. National Diabetes Statistics fact sheet: general information and national estimates on diabetes in the United States, 2005. Bethesda, MD: U.S. Department of Health and Human Services, National Institute of Health, 2005

²The National Kidney Foundation <http://www.kidney.org/kidneyDisease/>. Accessed February 14, 2006.

³Hogan P, et al, Diabetes Care 26:917–932, 2003.

amples of potential research payoffs include hepatitis C and diabetes complications. In the United States, hepatitis C infection affects an estimated 4 million people and is the leading cause of both liver cancer and liver failure due to end-stage cirrhosis. Patients who do not respond to standard medical therapy with interferon and ribavirin are at high risk of developing these severe health problems. Ideally, physicians should be able to predict likely “non-responders” to current therapy and those at risk for disease progression, and then tailor interventions to them. While this is not yet possible, ongoing studies will help to move the field forward, including a major clinical trial (HALT-C) aimed at preventing end-stage cirrhosis and lowering risk of liver cancer in “non-responders” with advanced disease.

Likewise, physicians would welcome new, precise methods for tailoring interventions to individuals with diabetes so as to reduce complications in those at greatest risk, while also lessening treatment burden. Landmark clinical trials have demonstrated that tight control of blood sugar levels in type 1 diabetes patients significantly reduces their overall risk of eye, kidney, nerve, and cardiovascular disease. Unfortunately, current therapies to achieve tight control also increase the risk of potentially life-threatening bouts of low blood sugar. If a simple method existed to identify patients who could tolerate “looser” control of blood sugar levels without an increased risk of complications, then therapy could be tailored accordingly. Pinpointing the underlying causes of diabetes complications will pave the way to such targeted interventions.

Developing a more personalized approach to medical therapy requires a robust toolkit forged from research advances. Therefore, the NIDDK is continuing with new initiatives to accelerate translation of fundamental research into clinically useful applications. For example, we want to be able to stop early scarring of the liver and kidney—known as fibrosis—before it ignites a series of events leading to irreversible organ failure. The NIDDK is fostering new, non-invasive imaging methods to reveal fibrosis. Such techniques will enable physicians to diagnose, monitor and treat liver and kidney disease more effectively. For diseases within the NIDDK mission, we are also committed to the discovery of biomarkers—factors, such as molecules, that can be measured and used to monitor a patient’s disease or response to therapy. A new translational initiative encourages research to develop and validate these biomarkers for clinical use.

Critically important for predicting and preempting chronic diseases—such as polycystic kidney disease (PKD), focal segmental glomerulosclerosis (FSGS), kidney stones, IC, IBD, IBS, non-alcoholic steatohepatitis (NASH), and hepatitis B and C—is a thorough understanding of their natural history. For example, discovery of PKD genes has led to insights into the molecular defect underlying most cases of this disease. Promising new medical therapies are being explored to prevent or reduce cyst formation, and new trials (HALT-PKD) will now test approaches for preventing progressive kidney damage. In the kidney disease FSGS, we do yet know all the causative factors, but a better understanding of FSGS progression has enabled the NIDDK to undertake a trial of therapies to prevent or delay kidney failure in patients. A new international patient registry should increase our understanding of inherited causes of calcium oxalate kidney stones. The cause(s) of the bladder disease IC remains unknown, but studies of a promising biomarker from urine may lead to improved diagnosis and treatment for patients, as well as to new therapeutic options.

Our efforts in digestive diseases will be guided by a long-range strategic research plan to be developed by a new National Commission, as well as by a recently completed Liver Disease Action Plan. We are already making progress on several fronts. In IBD, studies of a recently identified Crohn’s disease susceptibility gene are pointing the way to new therapeutic options. Researchers are exploring the multiple physical and cognitive factors that appear to play a role in IBS. A new clinical research network is studying the biological basis of progression from a less serious form of non-alcoholic fatty liver disease to the fatty liver, liver inflammation and scarring of NASH, and will test strategies to prevent disease progression in both adults and children. Studies of the hepatitis B virus continue in order to optimize treatment options. A new system to replicate (“grow”) hepatitis C virus in the laboratory will significantly enhance research to test potential therapeutic targets and open the door to vaccine development—complementing ongoing trials such as HALT-C.

Strikingly, research has revealed that obesity, with its comorbidities, is at the nexus of many chronic diseases. The high prevalence of obesity in the U.S. population, with nearly 31 percent of adults affected,⁴ bears directly on the millions affected with chronic diseases. Obese individuals are at increased risk of type 2 diabe-

⁴Flegal KM et al, JAMA 2002;288:1723–1727.

tes, and obesity is linked to increased risk of NASH, as well as of ESRD via type 2 diabetes and high blood pressure. However, not all overweight and obese individuals will develop obesity-associated diseases. Age, gender, race, ethnicity, socio-economic status, and individual genetics are among the many factors that may influence risk. Through initiatives developed by the NIH Obesity Task Force and through NIDDK-led efforts, we are encouraging research studies to promote prevention and to identify which subsets of obese individuals are at risk for developing particular comorbidities, and, in turn, to tailor interventions accordingly.

Recent data offer promise that we may be able to stem the tide of obesity-related health problems. For example, analyses by the United States Renal Data System (USRDS) indicate that overall incidence rates of ESRD have stabilized in the United States, following a 20 year period of annual increases. This finding suggests that there has been a successful translation into medical practice of research-based knowledge important to preventing ESRD—the use of medications (ACE inhibitors) and the benefits of controlling blood sugar and blood pressure levels. Unfortunately, this positive result has not yet been seen across the entire U.S. population, in that ESRD continues to affect minority groups disproportionately. The National Kidney Disease Education Program (NKDEP) has a major campaign aimed at reducing the burden of kidney disease in African Americans, for whom the risk factors of high blood pressure, diabetes, and a family history are dangerous red flags. Through its working groups, the program is also promoting the standardized, routine reporting of serum creatinine—an indicator of kidney function. Use of this simple approach can facilitate early detection and treatment of impending or active chronic kidney disease in patients. Along the same lines, the National Diabetes Education Program (NDEP) has translated into a multi-faceted campaign for multiple audiences the impressive results of the Diabetes Prevention Program (DPP) clinical trial. This trial demonstrated that lifestyle changes—relatively moderate weight loss and increased physical activity—can reduce the risk of type 2 diabetes by 58 percent in persons at risk for the disease.

Such hopeful results spur our efforts to further reduce the health burden of these chronic conditions through interventions to prevent obesity as early as possible. Prevention research needs to address the alarming rise in rates of pediatric overweight and obesity nationwide over the past three decades. A recent study indicates that approximately two million American adolescents have a prediabetic condition (IFG) strongly linked to obesity and overweight. Children and adolescents are being increasingly diagnosed with type 2 diabetes, NASH, and other obesity-associated conditions once found mainly in adults. To address key points of vulnerability early in life, the NIDDK is spearheading several initiatives, such as defining mechanisms by which maternal obesity and diabetes during pregnancy affect the future risk of obesity and other chronic diseases in offspring. Another initiative is focused on finding ways to prevent or manage weight gain in children. Moreover, the new “HEALTHY” trial will investigate whether a concerted, integrated program in middle schools will help reduce the prevalence of obesity-related harbingers of type 2 diabetes by improving cafeteria lunches, vending machine offerings, and physical education and promoting behavioral change. The tremendous success of the intensive lifestyle intervention for adults in the Diabetes Prevention Program provides hope that the HEALTHY trial may do the same for children.

The Nation’s investment in NIH-funded research offers enormous benefits, particularly the opportunity to preempt disease and reduce its lifelong costs, both human and economic. To this end, the NIDDK is harnessing new technologies, maximizing research investments, and capitalizing on new opportunities to achieve early, effective intervention for the many chronic diseases within its mission. Thank you, Mr. Chairman. I would be pleased to answer any questions that the Committee may have.

PREPARED STATEMENT OF DR. JOHN RUFFIN, DIRECTOR, NATIONAL CENTER ON
MINORITY HEALTH AND HEALTH DISPARITIES

Mr. Chairman and Members of the Committee: I am pleased to present the President’s budget request for the National Center on Minority Health and Health Disparities (NCMHD) for fiscal year 2007, a sum of \$194,299,000, which represents a decrease of \$1,106,000 over the comparable fiscal year 2006 appropriation.

The overall health of the general American population has improved; yet as a Nation we continue to be challenged by disparities in health among racial and ethnic minority and other health disparity populations. There continues to be a disproportionate burden of illness, disability and premature death resulting from diseases

and health conditions such as cancer, cardiovascular disease, HIV/AIDS, stroke, obesity, mental illness and diabetes, in these communities.

The cause of health disparities is multi-factorial in nature. The complexity of health disparities merits a strategic, innovative, and multi-faceted attack. Genes, biology, culture, race environment, socioeconomic, and health behaviors all contribute to this complex public health crisis. Biomedical research is essential in transforming the health of this Nation. In order to have the greatest impact on improving the health of America's underserved populations, at NIH, we believe a new biomedical research paradigm is needed—one that is predictive, personalized and preemptive. We need a well-coordinated, interdisciplinary effort involving traditional as well as non-traditional partners to get to the crux of the health disparities crisis.

The National Center on Minority Health and Health Disparities was established in 2000 to lead the Federal effort in health disparities research, research capacity building, and outreach. The NCMHD has always recognized the significance of partnerships in resolving health disparities. Our programs embody a strategy that emphasizes our efforts to build a biomedical research enterprise that is diverse, predictive, personalized, and preemptive.

The NCMHD is committed to training a diverse biomedical research workforce to examine issues relevant to the disparities in health of America's rapidly increasing racial and ethnic minority populations. More than 600 promising research scientists across the country have received NCMHD loan repayment awards to conduct health disparities research and clinical research. Institutional capacity building has been an important area of focus. Through our endowments and research infrastructure program, we have funded almost 40 academic institutions—more than half being minority-serving institutions. The funding is helping to equip the institutions, their faculty and students to engage in avant-garde biomedical research and training. Another integral element of our strategy is community participation. Our aim is to empower the community to address its own health problems. Our communities should include individuals other than patients, who must be actively engaged in research intervention and ultimately the translation and dissemination of research results into practical community tools.

Advancements in science and technology offer hope for the future. The NCMHD has supplied more than 100 individuals, institutions, and small businesses with resources to conduct research to help answer some of the perplexing issues in health disparities. NCMHD is one of the few NIH Institutes or Centers (IC) that focuses on populations and not specific diseases or health conditions. Consequently, we have had the unique opportunity of partnering with all of the ICs over the past five years in our quest to eliminate health disparities. Our partnerships and our programs have allowed us to support research into many of the diseases and health conditions affecting racial/ethnic minority and other health disparity populations. It is through these programs and partnerships, that the NCMHD has been able to have far reaching effect in improving the health of the Nation's health disparity populations. We have made progress, but there is much more to be achieved.

HEALTH DISPARITIES RESEARCH AGENDA

A national health disparities research agenda is fundamental in eliminating health disparities. Healthy People 2010, the prevention strategy for the Nation, identified a number of health objectives to be achieved over a 10-year period. The elimination of health disparities among different segments of the population in the United States is one of the goals. We have five years left as a Nation to demonstrate how far we have come in attaining that goal. The NIH through the leadership of the NCMHD has been a principal player in advancing the goals of Healthy People 2010. The NCMHD coordinates the development of the evolving NIH health disparities research agenda—the NIH Health Disparities Strategic Plan. The Plan represents the trans-NIH health disparities vision and strategy. Through the Strategic Plan, the NIH can aggressively address health disparities by fostering pioneering partnerships and initiatives. The NCMHD, through the Institute of Medicine (IOM), initiated the five-year evaluation of the NIH Health Disparities Strategic Plan. The NCMHD, in collaboration with NIH leadership and the Secretary of Health and Human Services will address the recommendations of the IOM report in implementing and reshaping the NIH health disparities research agenda.

NCMHD HEALTH DISPARITIES EFFORTS

At the NCMHD, we are working to build an inclusive, collaborative, and adaptive biomedical and behavioral research enterprise to identify innovative diagnostics, treatments, and preventive strategies that will eliminate health disparities. NCMHD activities have been numerous and far-reaching. The newest NCMHD ini-

tiative is the Community-Based Participatory Research (CBPR) Program, which supports 25 institutions nationwide. The CBPR exemplifies a predictive, personalized and preemptive approach to eliminating health disparities. It is a three-part program that engages the community in all phases of the research process and is directed to a specific disease/health condition in a particular minority population. It starts with a three-year planning grant, followed by a five-year grant to conduct intervention research, and concludes with a three-year grant to disseminate the research information. The CBPR is a novel approach for the biomedical research enterprise, and we anticipate its potential in addressing health disparities through projects such as: Project GRACE: A Participatory Approach to Address Health Disparities in HIV/AIDS among African American Population; Partnership to Overcome Obesity in Hawaii; Project AsPIRE (Asian American Partnership in Research); The Healing of the Canoe (is aimed at planning, implementing and evaluating a community-based and culturally competent intervention to reduce health disparities and promote health in the Suquamish Tribe reservation community); and Partnership for a Hispanic Diabetes Prevention Program in Washington.

The Centers of Excellence Program, "Project EXPORT" has been key in leading our effort in supporting the advancement of medical research and the transformation of the health care system. The program is creating new partnerships to enable institutions at all levels of capability to maximize their health disparities research, research training and community outreach efforts. The 73 Project EXPORT grantees have had a tremendous influence on creating more than 100 unique partnerships focused on health disparities. We have created an array of partnerships with entities such as hospitals; tribal groups; health plans; health centers; community and faith-based organizations; civic and non-profit health organizations; and local, city, and state governments. Biomedical research is important in understanding the underlying causes of health disparities, and how to prevent, diagnose and treat disease and disability. The research conducted by our Centers of Excellence will help to increase that understanding through projects such as: Perceived Discrimination in Healthcare among American Indian/Alaska Natives; Religious Outlook on Organ and Tissue Sharing; Inflammation and Asthma; Impact of Coronary Heart Disease Risk Perception on Health Behaviors and Physical Activity Assessment in Multi-Ethnic Women.

The NCMHD Loan Repayment Programs support the goals of the new NIH Pathway to Independence Program by increasing the number of qualified health care professionals who conduct health disparities and clinical research. The programs promote a diverse and strong scientific workforce. Since its establishment, the Loan Repayment Program has made more than 600 new awards to researchers in research disciplines such as epidemiology, pharmacology, linguistics, etiology, health policy, and behavioral science. The program is fulfilling its Congressional intent with the majority of award recipients being from a health disparity population. The NCMHD is training research scientists and health professionals not only to deal with health disparities on the domestic level, but also globally. Through the Minority Health and Health Disparities International Research Training Program (MHIRT), 24 academic institutions have developed international training opportunities in health disparities research for faculty and students. MHIRT participants will be exposed to research areas including cancer epidemiology, reproductive biology, parasitology, and ethnopharmacology in countries such as Ethiopia, Ghana, Jamaica, Dominican Republic, Australia, and Spain.

The NCMHD commitment to enhancing research capacity at academic institutions is best demonstrated through its Research Endowment Program and its Research Infrastructure in Minority Institutions (RIMI) Program. The RIMI program is building research capacity in 21 predominantly minority-serving academic institutions. The NCMHD provides endowment grants to eligible institutions to build minority health and other health disparities research and training capacity. The Endowment program has funded 16 institutions to strengthen teaching programs in the biomedical and behavioral sciences; establish endowed chairs and programs; obtain state-of-the-art equipment for instruction and research; and enhance the recruitment and retention of student and faculty from health disparity populations.

RESEARCH COLLABORATIONS

The health disparities phenomenon is almost incomprehensible until it is humanized. Hurricane Katrina demonstrated the underlying national health crisis that continues to plague America's racial and ethnic minority and low-socio economic communities. In some cases, evacuees received medical treatment for the first time for chronic and life-threatening diseases, such as hypertension, cardiovascular diseases, diabetes, and mental health disorders.

Community involvement and partnerships are critical to redress the devastation experienced by individuals caught in the path of Hurricane Katrina. The NCMHD is collaborating with the HHS Office of Minority Health on a HHS \$12 million initiative to bring desperately needed health care services, information, and hope to racial and ethnic minority populations in the Gulf Coast region. The NCMHD provided \$5.2 million in funding to support that initiative. Our Centers of Excellence have also been mobilized to participate in the initiative to create a Regional Coordinating Center to build a research infrastructure for on-going efforts to eliminate health disparities in the hurricane-ravaged communities. Such an infrastructure would integrate research-based academic facilities, public health, primary care, and specialty care officials to engage in innovative approaches to relief activities, including developing and testing culturally relevant telemedicine response to mental health needs, and other acute and chronic diseases; instituting electronic health records for individuals in the region through partnerships with academic experts in practice-based research; and establishing effective community-based screening and surveillance systems to monitor health needs of individuals evacuated from hurricane-ravaged communities, as well as those returning to communities as they are re-built, with a special focus on exacerbations of existing health disparities.

The NCMHD Visiting Faculty Program is a new program that is assisting researchers displaced by the hurricane. The program will help to bring displaced scientists who were employed at institutions in the Gulf Coast states to the NIH, so that they can continue their research efforts.

CONCLUSION

During its initial five years the NCMHD has strived to be inclusive, creative, and adaptable to changing circumstances. The programs highlighted are but some examples of what is being done to eliminate health disparities. We need to build on these successes and further our activities. Toward this end, the NCMHD will sustain and expand its primary strategies. Research capacity building will continue to extend beyond academia to involve community and faith-based organizations, individuals, and businesses at the local and grassroots level. Training and the diversification of the health, scientific, and technological workforce will remain key areas of focus in developing innovative projects. Prevention, treatment, cultural competency, and healthcare delivery for urban and rural communities will continue to be approached aggressively.

Through our vision of the future embodied in the NIH Health Disparities Strategic Plan, the NCMHD renews its commitment to build a solid and diverse national biomedical research enterprise of individuals and institutions dedicated to eliminating health disparities. With our NIH Institute and Center collaborations and our partnerships with scientific institutions and community-based organizations across the Nation, the NCMHD will advance scientific discovery to ensure the health of all Americans. All citizens should have an equal opportunity to live long, healthy and productive lives.

PREPARED STATEMENT OF DR. DAVID A. SCHWARTZ, DIRECTOR, NATIONAL INSTITUTE OF ENVIRONMENTAL HEALTH SCIENCES

Mr. Chairman and Members of the Committee: I am pleased to present the President's budget for the National Institute of Environmental Health Sciences (NIEHS) for fiscal year 2007, a sum of \$637,323,000 which reflects a decrease of \$3,809,000 from the fiscal year 2006 appropriation.

INTRODUCTION

As the Director of NIEHS, I am grateful for this opportunity to present our vision for the Institute and environmental health sciences. Our vision at NIEHS is to prevent disease and improve human health by using environmental sciences to understand human biology and human disease. Environmental agents contribute to many conditions of public importance, including cancer, neurodevelopmental disorders, autoimmune diseases, and chronic lung disease. While many of our investigators are focused on understanding the causes of disease, we are also involved in studies of susceptibility, basic mechanisms of disease, and identifying novel approaches to intervention and disease prevention.

Recent NIEHS-supported research illustrates the range of our Institute's science. In studying asthma, NIEHS scientists examined the mechanisms controlling the body's own system for achieving balance between airway constriction and airway relaxation. They discovered a natural bronchodilator, deficient in asthmatics, that re-

laxes the airway; absence of this enzyme in mice increases the development of allergen-induced asthma. In other work, investigators studied the role of supplements in preventing birth defects. While folate has been shown to prevent spina bifida, a defect in the spinal column, epidemiologists have now discovered that women who take folate supplements during pregnancy are at reduced risk of giving birth to a child with cleft lip and palate birth defects. Finally, NIEHS-supported studies have shown that short-term exposure to ozone can increase mortality rates. These studies demonstrated that a 10-part per billion (ppb) increase in the previous week's ozone was associated with a significant increase in cardiovascular and respiratory mortality.

CURRENT CHALLENGES

Today, we find ourselves at a critical junction where new tools and opportunities for substantial scientific achievement intersect with our growing understanding of cellular and molecular mechanisms by which environmental exposures exert their effects. Our challenge is to take advantage of these advances and to forge new frontiers to improve our nation's health. To help ensure that the best opportunities are identified and funded, we have made several programmatic and scientific changes at the Institute since last April. Importantly, these changes are consistent with our strategic plan that we initiated ten months ago and have involved the efforts of many talented individuals across the country. Concurrently, we are engaged in developing critical partnerships to address areas of public health concern that involve the missions of multiple organizations.

INTEGRATIVE RESEARCH ON HUMAN DISEASE

Environmental health science is not limited to an organ system, disease or population, but spans the full spectrum of human health and disease. The interdisciplinary nature of our work requires the right mix of specialists. As NIEHS increases its focus on common human diseases, interdisciplinary teams of scientists will be needed to integrate clinical, epidemiological, and toxicological research with basic mechanistic studies. To optimize the creation of these interdisciplinary research teams, I have begun a number of programmatic changes. I have created an Office of Translational Biomedicine that will re-focus the NIEHS intramural and extramural programs so that our basic research discoveries can be rapidly applied to improvements in human health. In our division of extramural research, I have initiated a new program, DISCOVER (Disease Investigation for Specialized Clinically Oriented Ventures in Environmental Research), that brings together extramural scientists with expertise in basic, clinical, and population-based research to focus on a disease related to environmental exposures. Among intramural investigators, I have developed a new program, the Director's Challenge, that also supports multidisciplinary research teams to attack basic problems, like inflammation and oxidative stress, that can be induced by environmental exposures and can influence the development of many different diseases. I am re-engineering our Environmental Health Science Research Centers so that they include a clinical component in their research, thus enhancing the disease focus and relevance of these centers. I have also directed funds to build a new clinical research unit on campus so that our intramural research program can be integrated into human biology and human disease.

RECRUIT AND TRAIN THE NEXT GENERATION

A more integrative approach to understanding complex human diseases will require innovative scientists with the type of training that can take advantage of new technologies and research opportunities. NIEHS has initiated a number of changes that address our future workforce needs. We have re-engineered our existing training programs so that we can better identify and encourage promising students at all levels to pursue careers in environmental health research. The existing T32 training grants program will be broadened to include other training opportunities in interdisciplinary research and genetics and genomics. We will also train physician-scientists by expanding our MD, PhD training program and by supporting young investigators in their transition to early faculty positions (developed a K12 training program). We have also instituted the Outstanding New Environmental Scientist, or ONES, award to help young, talented investigators make the transition from mentored to independent research. These grants will assist young scientists in launching innovative research programs focusing on problems of environmental exposures and human biology, human pathophysiology, and human disease by providing support for both the research and the start-up costs that are needed to establish a laboratory.

EXPAND COMMUNITY-LINKED RESEARCH

The likelihood of exposure to environmental agents increases in economically disadvantaged communities and is associated with an excess disease burden in these communities. The NIEHS traditionally supports research relevant to understanding those health disparities and community concerns. We will continue to support research, both domestically and globally, that can offer insights into how to reduce exposures and disease in these settings. We will also be involved in developing quick responses to emerging environmental health issues, such as arose in the aftermath of Hurricane Katrina, when NIEHS launched a website that used a Global Information System to assess environmental hazards caused by the storm, as well as coordinated a local team of physicians and support staff to deliver medical care. Beginning in fiscal year 2006, NIEHS is planning to support a research program to investigate the health consequences of Hurricane Katrina. This project will examine the role of genes, the environment, and gene-environment interaction in the exacerbation of airway disease from exposure to mold and microbial toxins in New Orleans following Hurricane Katrina.

RE-EVALUATE PROGRAMMATIC INVESTMENTS

We have decided that investigator-initiated research needs to be prioritized at NIEHS and are rigorously re-evaluating other existing programs and approaches to determine if we need to re-conceptualize or eliminate some of these efforts. We have developed two new programs aimed at using environmental agents to understand basic mechanisms in human biology. One is the Epigenetics Initiative which explores intrauterine environmental and nutritional factors that can alter gene expression and generate developmental abnormalities or functional changes. The other is the Comparative Biology of Environmental Disease which uses novel “-omics” technologies and comparative biology approaches to study environmentally-relevant disease pathways. These studies will help us understand why people exposed to the same environmental stressors respond differently. Finally, we have reorganized the National Center for Toxicogenomics to insure a more timely and relevant product. In order to achieve these new programs and priorities, I have decided that the Comparative Mouse Genomics Centers Consortium has fulfilled its mission of infrastructure development and will not be re-competed.

GENE, ENVIRONMENT AND HEALTH INITIATIVE—A NOVEL PARTNERSHIP

Currently, we have inadequate techniques to precisely measure environmental exposures. This situation is in marked contrast to the robust tools that have been recently developed for the fields of genetics and genomics. To be able to assess the role that environmental exposures and genetic variation play in the risk of developing disease, we simply need more robust tools to measure the environmental exposures and the biological responses to these agents. While these tools are absolutely vital in moving the field of environmental health sciences forward, these tools will be invaluable to investigators in all areas of biomedical research. To further this goal, the NIH, with the support of the Secretary, has developed the Gene, Environment and Health Initiative. Our goal in this initiative is to develop tools to precisely measure individual biological responses to changes in our environment, diet, and activity level so that we can understand the relationship between various environmental exposures and human health and disease.

NIEHS STRATEGIC PLAN—A NEW OUTLOOK

The NIEHS recently embarked on a strategic planning exercise, the final version of which can be viewed on our website and will soon be distributed in hardcopy. This document represents the efforts of many scientists and advocacy groups. I have been gratified by the intense interest and involvement from citizens and scientists throughout the country. This document is truly a national plan that represents our collective wisdom of where environmental health sciences needs to go in order to reap full benefit of our investments and opportunities. Many of the suggestions have already been incorporated into our new programs and we will continue to design programs that are responsive to this plan.

SUMMARY

The opportunities within environmental health sciences are greater than they have ever been. With our recent nationally supported strategic plan and the exciting partnerships that we are developing, it is my belief that environmental health sciences will continue to strengthen. With an improved relevance to major public health concerns, better technology for teasing out important environmental contrib-

utors to disease, an integrated approach to research, and a re-energized workforce, I expect the NIEHS to provide many of the important scientific advances of the future. Ultimately, this knowledge will be used to reduce the burden of many important diseases both in this country and abroad. I would be happy to answer any questions you might have.

PREPARED STATEMENT OF DR. PAUL A. SIEVING, DIRECTOR, NATIONAL EYE INSTITUTE

Mr. Chairman and Members of the Committee: I am pleased to present the fiscal year 2007 President's budget request for the National Eye Institute (NEI). The fiscal year 2007 budget includes \$661,358,000, which reflects a decrease of \$5,398,000 under the fiscal year 2006 enacted level of \$666,756,000 comparable for transfers proposed in the President's request.

As the Director of the NEI it is my privilege to report on the progress laboratory and clinical scientists are making in combating blindness and visual impairment and about the unique opportunities that exist in the field of vision research.

RETINAL DISEASES

Retinal diseases are a diverse set of sight-threatening conditions that include age-related macular degeneration (AMD), diabetic retinopathy, retinopathy of prematurity, retinitis pigmentosa, Usher's syndrome, ocular albinism, retinal detachment, uveitis (inflammation) and cancer (choroidal melanoma and retinoblastoma).

Of these diseases, AMD is the most frequent cause of vision loss and legal blindness in older-age Americans, making it a research priority for the NEI. AMD causes degeneration of the macula, the central part of the retina that gives us fine, sharp visual detail. AMD is thought to result from the confluence of genetic predisposition and chronic exposure to environmental risk factors.

On the genetic side of the equation, identifying subtle alterations in a gene or genes in AMD and other late onset diseases has been complicated by the fact that traditional genetic research strategies and tools are either inadequate or too cumbersome in their application. The development of more sophisticated genetic tools has enabled scientists to scan the entire human genome more quickly and efficiently. Using data from the Human Genome Project and the International HapMap Project, four different NEI supported laboratories identified a common variation in a gene called complement factor H (CFH) that accounts for an estimated 50 percent of the risk of developing AMD.

The CFH protein regulates an inflammatory response that is typically triggered by infectious microbes. Alterations in the CFH gene are postulated to poorly regulate this response, leading to chronic, localized inflammation and ensuing damage to cells in the center of the retina, the macula, and its neighboring tissues. Inflammation is thought to play a role in many other common diseases such as Alzheimer's disease, Parkinson's disease, multiple sclerosis, kidney disease, stroke, and atherosclerosis. Although the cells, tissues, and molecular events in these diseases are diverse, they may share some common disease mechanisms that present an opportunity to cross pollinate findings from diverse research areas.

The discovery of the CFH gene will allow researchers to create animal models and evaluate therapies that control chronic inflammation. The CFH gene also illustrates the potential of a new paradigm for medicine in the 21st century. This new paradigm holds that the practice of medicine should be preemptive, personal and predictive. The CFH gene presents the possibility to one day identify at-risk patients and intervene well before pathology is clinically detectable.

STRABISMUS, AMBLYOPIA AND VISUAL PROCESSING

Developmental disorders such as strabismus (misalignment of the eyes) and amblyopia (commonly known as "lazy eye") are among the most common eye conditions that affect the vision of children. It is estimated that 20 percent of preschool children ages 3-4 have these and other treatable eye conditions.¹

In an effort to identify children with treatable eye conditions, many states are developing guidelines for preschool screening programs. However, none of the commonly used vision tests have been evaluated in a research-based environment to establish their effectiveness. To address this issue, the NEI supported a large, multi-center study called the Vision in Preschoolers (VIP) Study to determine which tests and test conditions can effectively identify preschoolers in need of a comprehensive

¹ Comparison of preschool vision screening tests as administered by licensed eye care professionals in the Vision in Preschoolers Study. *Ophthalmology* 111(4):637-50, 2004.

eye exam. Previously VIP Study researchers found that in the hands of licensed eye care professionals, the best performing tests were able to detect 90 percent of children with the most severe visual impairments. This year, VIP Study investigators found that specially trained nurses and lay people can achieve results that are comparable to screenings performed by licensed eye care professionals. Given that most eye screening programs rely on lay people and nurses, this finding validates the effectiveness of this approach.

GLAUCOMA AND OPTIC NEUROPATHIES

Glaucoma is a group of eye disorders that causes optic nerve damage that can lead to severe visual impairment or blindness. Elevated intraocular pressure (IOP) is frequently, but not always, associated with glaucoma. Glaucoma is a major public health problem and published studies find that the disease is three times higher in African Americans than in non-Hispanic whites.²

The defining event that leads to vision loss in all forms of glaucoma is the degeneration of retinal ganglion cells (RGC) in the back of the eye. These cells relay visual information to the brain through the optic nerve and their loss effectively severs the neural network that allows us to process visual information. However, little is known about the molecular events that result in RGC degeneration. Using high dose radiation and bone marrow rescue to explore inflammatory responses in an animal model of glaucoma, researchers unexpectedly discovered that this procedure prevents the loss of RGCs. The neuroprotection offered by this procedure was complete, highly reproducible, and lasting. Normally, by 12–14 months, these glaucoma susceptible mice have complete RGC loss. At 14 months, treated mice had no detectable signs of disease. Although the mechanism that offers neuroprotection is not yet known, researchers speculate that it is due to radiation, because the transferred bone marrow was genetically identical to the original bone marrow the mice were born with. This highly novel treatment protocol offers a tool to understand neurodegeneration and, with refinement, could have important implications for the treatment and prevention of neurodegenerative diseases.

CORNEAL DISEASES

The cornea is the transparent tissue at the front of the eye. Corneal disease and injuries are the leading cause of visits to eye care professionals, and are some of the most painful ocular disorders. In addition, approximately 25 percent of Americans have a refractive error known as myopia or nearsightedness that requires correction to achieve sharp vision; many others are far-sighted or have astigmatism.³

Inflammation is a common immune response to injury and infection in the body. In the cornea, however, inflammation can cause extreme discomfort and result in vision loss. Nonetheless, the cornea retains a remarkable capacity for wound repair while actively suppressing an inflammatory response. Scientists have recently discovered that two lipids, lipoxin A₄ (LXA₄) and docosahexaenoic acid-derived neuroprotectin D1 (NPD1), are formed in the cornea and act as anti-inflammatory agents during corneal infection and wound healing. Topical treatment with LXA₄ and NPD1 in mice with corneal injuries increased the rate of tissue repair and inhibited inflammation without impairing the recruitment of key immune leukocytes, which are normally associated with inflammation, into the wounded tissue. Moreover, a transgenic mouse that lacks these lipids exhibited delayed wound healing and attenuated leukocyte recruitment. The identification of these anti-inflammatory lipids in the cornea and their enhancement of wound healing by topical application suggest their use as therapeutic agents to overcome aberrant and damaging inflammatory responses in the eye.

CATARACT

Cataract, an opacity of the lens of the eye, interferes with vision and is the leading cause of blindness in developing countries. In the United States, cataract is also a major public health problem. The enormous economic burden of cataract will worsen significantly in coming decades as the American population ages.

The lens is a dense, compact structure containing two cell types: metabolically active epithelial cells and quiescent fiber cells. Throughout the life-time of an individual, the lens carries out a process of continued growth with epithelial cells divid-

²The Eye Diseases Prevalence Research Group: Prevalence of open-angle glaucoma among adults in the United States. *Arch Ophthalmol* 122:532–538, 2004.

³The Eye Diseases Prevalence Research Group: The prevalence of refractive errors among adults in the United States, Western Europe, and Australia. *Arch Ophthalmol*. 122:495–505, 2004.

ing and differentiating into fiber cells. During this process, the emerging fiber cells become denuded of organelles such as the nucleus and mitochondria. This process in part helps the lens achieve the high transparency needed for clear vision. Scientists have previously found that the lens uses proteins involved in a biological process called programmed cell death or apoptosis to rid lens fiber cells of their organelles. This past year, vision researchers have discovered the biologic process that regulates apoptosis such that it allows for the elimination of organelles without resulting in cell death.

The process is termed Apoptosis-related Bcl-2 and Caspase-dependent (ABC) differentiation. In this process, a number of proteins that normally lead to cell death such as caspases—proteins that break-down internal cellular structures—are expressed to denude organelles. The caspase proteins are balanced by the simultaneous induction of pro-survival molecules such as bcl-2, a protein that binds to cell death proteins and inhibits further damage or death to fiber cells. The discovery of ABC differentiation in the lens will allow researchers to better understand lens cell renewal and determine whether faulty mechanisms in this process might lead to cataract formation.

NIH ROADMAP

A goal of the NIH Roadmap Nanomedicine Initiative is to characterize quantitatively the molecular scale components or nanomachinery of cells and to precisely control and manipulate these molecules and supramolecular assemblies in living cells to improve human health. The NEI has a leadership role in implementing the NIH Roadmap Nanomedicine Initiative. Under this initiative, a Request for Applications (RFA) was prepared to award Nanomedicine Center Concept Development Awards. These concept development awards were created to allow applicants time and resources to develop the concept for a Nanomedicine Center that would address various issues in nanomedicine including, biomolecular dynamics, intracellular transport, and protein-protein interactions. Understanding these fundamental biologic processes at the nanoscale level will allow scientists to engineer molecular structures, assemblies, and organelles for treating diseased or damaged cells and tissues. Of the applications, four Nanomedicine Centers were awarded in fiscal year 2005. The Centers will be dedicated to understanding the nanobiology that underlies protein folding machinery; ion channels and ion transport proteins; synthetic signaling and motility systems; and mechanical biology. The NIH expects to fund additional Nanomedicine Centers in fiscal year 2006. The Nanomedicine Initiative will also benefit eye research in a more direct way. Current NEI grantees are exploring the use of nanotechnology to assist in corneal wound healing and drug delivery to the retina. Increased support of nanomedicine through the NIH Roadmap will undoubtedly speed progress in these areas.

NIH NEUROSCIENCE BLUEPRINT

The NIH Neuroscience Blueprint is a collaborative effort among 15 NIH institutes and centers to accelerate the pace of discovery and understanding in neurosciences research. In an effort to better understand all elements of the nervous system, the Blueprint will focus on the development of tools and resources that will facilitate research on the processes of development, neurodegeneration, and plasticity that underlie the health and disorders of the nervous system. One of the approaches to develop these tools and resources is a cellular level approach to discovering the key molecules involved in nervous system function. There is still a need to identify the location, the developmental timing, and the cellular function of most of the genes and proteins expressed in the brain. Mapping of the neurogenome is being conducted by creating and analyzing transgenic mice to map gene expression and activity to different cell types and regions of the mouse central nervous system. The NEI component of this effort will be to ensure that the genes involved in neurons of the complete visual system are included in the neurogenome map.

Mr. Chairman, this concludes my prepared statement. I would be pleased to respond to any questions you or other members of the committee may have.

PREPARED STATEMENT OF DR. STEPHEN E. STRAUS, DIRECTOR, NATIONAL CENTER FOR COMPLEMENTARY AND ALTERNATIVE MEDICINE

Mr. Chairman and Members of the Committee: I am pleased to present the President's fiscal year 2007 budget request for the National Center For Complementary And Alternative Medicine (NCCAM). The fiscal year 2007 budget includes

\$120,554,000, a decrease of \$911,000 over the comparable fiscal year 2006 appropriation of \$121,465,000.

NCCAM has made significant progress in discovering the potential of complementary and alternative medicine (CAM) to prevent and treat disease. During NCCAM's first 7 years, the Center has formed a research enterprise that addresses the challenges of conducting CAM research as well as training investigators, conducting outreach, and facilitating the integration of proven CAM therapies into the health care that Americans receive.

SETTING THE COURSE

Through national surveys, we know that two-thirds of Americans are using some form of CAM each year. We are gaining understanding of which Americans use the various CAM modalities and for which health purposes. These patterns of CAM use will inform NCCAM's research priority setting in fiscal year 2007, along with guidance from two key documents:

- The NCCAM Strategic Plan for 2005–2009 (developed with input from the public and scientific and medical communities nationwide); and
- The Institute of Medicine's 2005 report, "Complementary and Alternative Medicine in the United States."

In fiscal year 2007, NCCAM will again collaborate with the Centers for Disease Control and Prevention to support the National Health Interview Survey to capture changes in trends of the American public's use of CAM.

FURTHERING THE RESEARCH MISSION

Seven years of NCCAM investments in CAM research translate to the support of more than 1,200 projects (in research, training, and career development) at over 260 U.S. institutions. There has been a 20-fold increase in the number of CAM papers published in leading scientific journals by NCCAM grantees. In fiscal year 2007, building upon this strong foundation, NCCAM plans to further enhance CAM research in the following areas.

A Flourishing Centers Program

NCCAM has expanded and refined its approach to research centers. As a result, the Center now has a diverse cadre of multidisciplinary research centers at conventional and CAM institutions nationwide.

- Centers of Excellence for Research on CAM.*—Six centers with outstanding research records direct teams of CAM and conventional investigators to explore, using cutting-edge technologies, how CAM therapies may work.
- Developmental Centers for Research on CAM.*—Scientists and practitioners at 18 CAM and conventional institutions have forged research partnerships. In fiscal year 2007 there will be new Phase I developmental centers for CAM institutions just launching programs of research, and Phase II developmental centers for CAM institutions prepared to undertake more sophisticated research studies.
- International Centers for Research on CAM.*—Two centers support U.S. investigators who collaborate with experts in the traditional medical systems of their own countries, building research expertise and capacity abroad and providing foreign researchers with valuable experience in navigating the NIH grants system.
- Botanical Research Centers.*—Seven dietary supplement research centers focusing on studies of botanical products are funded by NCCAM and the NIH Office of Dietary Supplements. Research conducted by these centers will advance the scientific base of knowledge about the safety, effectiveness, and mechanisms of action of botanicals.

Studies of Herbs and Other Dietary Supplements

Herbs and other dietary supplements are widely used by the American public and they are a research priority for NCCAM. Studying botanicals, however, has presented special research challenges related to product characterization, standardization, and dosage. With the advice of experts in herbal medicine and leaders of the dietary supplement industry, NCCAM is improving product consistency for research studies and thus increasing the probability that the studies NCCAM funds will yield accurate findings.

In this regard, the Center has developed research-quality cranberry products to use in studies of urinary tract infections and standardized an extract of milk thistle (silymarin), for study in patients with chronic viral hepatitis and non-alcohol-related steatohepatitis, a collaborative project with the National Institute of Diabetes and Digestive and Kidney Diseases.

NCCAM has worked with several NIH partners to design, conduct, and fund large clinical trials of dietary supplements. The largest of these was reported in February 2006 in the *New England Journal of Medicine*: a 4-year study (co-funded by the National Institute of Arthritis and Musculoskeletal and Skin Diseases) of glucosamine and chondroitin sulfate, two dietary supplements widely used by people with knee osteoarthritis. In this study, the two supplements combined did not provide statistically significant pain relief for all the participants, compared to placebo. However, a small subset of participants with moderate-to-severe pain had significant pain relief. An ancillary study is continuing to determine whether the combination of these supplements can prevent or delay further joint deterioration, a common long-term outcome for people with osteoarthritis.

A Broad Research Portfolio

There are hundreds of different practices, products, and approaches that comprise CAM. Thus, the research that NCCAM funds is wide-ranging. Areas that NCCAM will emphasize further in fiscal year 2007 include:

- Manual therapies*.—The mechanisms of action underlying the effects of manipulative and body-based therapies such as chiropractic and massage are little understood. Therefore, NCCAM is launching an initiative in fiscal year 2007 on the biology of manual therapies to better understand the effects of these techniques on the body.
- Mind-body medicine*.—One recent NCCAM-funded study found that tai chi combined with standard medical care benefits patients with chronic heart failure. Studies of meditation and mindfulness-based stress reduction in various health conditions are under way. NCCAM is also redirecting the focus of its intramural research program to emphasize studies of mind-body medicine.
- Echinacea*.—Research on echinacea is being done both because of the public health burden of the common cold and the public's widespread use of this natural product. A study of a single dosage of *Echinacea purpurea* to treat viral colds in healthy children was recently completed by an NCCAM grantee. A larger study is being undertaken in which a range of doses of this popular herb will be assessed for its ability to prevent colds in children.
- Immune responses*.—Many CAM interventions are believed to affect the immune system, either by enhancing its ability to thwart infection or by suppressing an overactive response, as occurs in autoimmune diseases. NCCAM is exploring the immune effects and basic mechanisms of action of various CAM modalities such as traditional Chinese herbal mixtures, ginseng, green tea, and *Ginkgo biloba*.

EXPANDING TRAINING AND CAREER DEVELOPMENT

There can be no significant CAM research progress without a sufficient cadre of investigators who are both skilled in rigorous research and knowledgeable about CAM practices. NCCAM has increased the number, quality, and diversity of the CAM research community using a variety of approaches and grant mechanisms. In fiscal year 2007, NCCAM will offer three new training opportunities: supplements to existing research grants, in order to attract more CAM practitioners into research endeavors; the CAM Practitioner Research Career Development Award, for CAM practitioners interested in research; and the NCCAM Career Transition Award, to help outstanding postdoctoral research fellows in their transition to an independent career in CAM research.

DISSEMINATING INFORMATION

From the outset, NCCAM has made it a priority to help practitioners, patients, and the public make informed decisions about CAM. The Center conducts outreach to public and professional audiences through a variety of channels: information clearinghouse, website, quarterly newsletter, conferences, Distinguished Lecture Series, and online continuing education. With the National Library of Medicine, the Center publishes CAM on PubMed, an online database of more than 400,000 research papers on CAM.

FACILITATING INTEGRATION

NCCAM is committed to facilitating the integration of safe and effective CAM therapies into conventional medicine. One example of this effort is within the NIH itself. The Center is establishing a new Integrative Medicine Consult Service at the NIH Clinical Center, to provide integrative medical consultations and enrich patient care. In addition, NCCAM continues to provide CAM curriculum development grants to conventional medical, dental, and nursing schools.

COLLABORATING ACROSS NIH

NCCAM continues its collaborations with other NIH Institutes and Centers, as a contributing member of the biomedical research community. For example, NCCAM is a partner in several of the NIH Roadmap for Medical Research initiatives, including the Exploratory Centers for Interdisciplinary Research. Also, by participating in efforts like the NIH Neuroscience Blueprint, the NIH Pain Consortium, and the Trans-NIH Obesity Initiative, NCCAM can accelerate efforts to unlock the potential of CAM therapies through these multidisciplinary research initiatives.

LOOKING TOWARD THE FUTURE

Mindful of the lessons learned in our first 7 years as an NIH Center, and with growing understanding of the scientific opportunities and public health priorities to be addressed with CAM approaches, NCCAM will continue to explore options to sustain and improve the health and well-being of the American people.

Thank you, Mr. Chairman. I would be pleased to answer any questions that the Committee may have.

PREPARED STATEMENT OF DR. LAWRENCE A. TABAK, DIRECTOR, NATIONAL INSTITUTE OF DENTAL AND CRANIOFACIAL RESEARCH

Mr. Chairman and Members of the Committee: I am pleased to present the President's budget request for the National Institute of Dental and Craniofacial Research (NIDCR) for fiscal year 2007. The fiscal year 2007 budget includes \$386,095,000, a decrease of \$3,241,000 from the fiscal year 2006 level of \$389,336,000, comparable for transfers proposed in the President's Request.

STRENGTHENING THE EVIDENCE BASE IN DENTAL CARE

Health care decisions should be guided by the preponderance of clinical research data, or evidence, whenever possible. This approach is known as "evidence-based medicine", a concept that has evolved into a driving force in healthcare.

Recognizing the concept's value, dentistry also has embraced an evidence-based approach. Yet, having sufficient clinical data from which to build that base can be challenging. For some oral health problems, evidence-based approaches are possible; for many others, knowledge gaps must be filled before an evidence-based approach can take root. As the nation's leading supporter of oral, dental, and craniofacial research, the NIDCR is uniquely positioned to fill those gaps while continuing its efforts in the laboratory to develop new and even more effective ways to prevent, diagnose, and treat dental diseases. I would like to highlight over the next few minutes how the NIDCR is sowing the clinical seeds of progress to advance evidence-based dentistry in America and, above all, improve the nation's oral health.

PRACTICE-BASED RESEARCH NETWORKS

Healthcare providers sometimes comment that too often they are not included as participants in research, noting that their clinical experience and insight are significant assets to understand and address patients' most pressing health concerns. I believe that there is much to be gained from engaging clinical practitioners in research. That is why the NIDCR recently established three regional practice-based research networks (PBRNs) to investigate everyday issues in oral healthcare.

Each PBRN involves 100 or more oral health practitioners who will propose and conduct studies of common dental procedures across a range of patient and clinical conditions. For example, some of the early investigations will gather data on methods dentists use to restore teeth with deep decay, and to assess caries risk. Each network will conduct 15 to 20 clinical studies over the next seven years. The PBRNs also will collect information to generate data on disease, treatment trends, and the prevalence of less common oral conditions.

While the PBRNs aim high, their success will be rooted in their focus on real-world clinical issues and their ability to generate information that will be of immediate value to practitioners and patients alike. The studies will involve topics and procedures that clinicians themselves identify as relevant and in need of systematic research to help guide clinical decisions. I believe the PBRNs have the potential to generate a body of high quality clinical research data in a relatively short period of time. Most importantly, their research will substantially enhance the base of evidence clinicians can use to inform treatment decisions, translate newer information into daily practice, and directly affect and improve routine dental care.

GREATER EMPHASIS ON LARGE CLINICAL STUDIES

The nation's progress against heart disease, cancer, and infectious diseases has been accelerated by large clinical studies yielding results that can be generalized and can clarify the interplay of many variables. In dentistry, clinical research traditionally has involved smaller studies with fewer participants. The NIDCR is changing this trend by supporting larger clinical studies whose outcomes have the potential to fundamentally change dental practice and improve public health. I would like to tell you about some examples.

PERIODONTAL DISEASE AND PRETERM BIRTH

In the United States, about one in eight babies is born prematurely.¹ Preterm babies can be so small and underdeveloped that they must remain hospitalized for months and, if they survive, spend years battling chronic health problems. This heartbreaking situation has spurred scientists to identify risk factors associated with premature births. Risk factors such as smoking, hypertension, and diabetes allow doctors to identify women who are more likely to deliver prematurely and to tailor their prenatal care. However, identification of risk factors is a work in progress. One in four of preterm births (more than 125,000 per year) occurs without any known explanation.² Scientists have assembled an intriguing body of preliminary evidence to suggest that women who have severe gum, or periodontal, disease during pregnancy are at increased risk of preterm delivery. This raises the question: Does treatment for periodontal disease during pregnancy help women reach full term and give birth to healthy babies?

The NIDCR is supporting the first large, controlled Phase III clinical trials to answer this important public health question. Two studies involve over 2,600 women of various racial, ethnic, and economic backgrounds. The first, called the Obstetrics and Periodontal Therapy (OPT) trial, will soon report its findings, providing for the first time the clinical data needed to offer sound scientific advice on this issue. The results of the second study, called the Maternal Oral Therapy to Reduce Obstetric Risk (MOTOR) trial, should be forthcoming next year.

BETTER PAIN TREATMENTS FOR JAW CONDITION

Temporomandibular joint and muscle disorder (TMJMD) is an umbrella term for conditions affecting the area in and around the temporomandibular joint, or TMJ. The TMJs connect the jaw to the skull. Common symptoms of TMJMD include persistent pain in the jaw muscles, restricted jaw movement, and jaw locking.

Although TMJ disorders vary in their duration and severity, for some people the pain becomes severe and permanent. NIDCR recently launched a large, seven-year clinical study to accelerate research on better pain-control treatments for TMJMDs. The study, called Orofacial Pain: Prospective Evaluation and Risk Assessment (OPPERA) will collect data on 3,200 healthy volunteers for three to five years to see how many develop TMJMD, opening a largely unexplored window from which to observe the early stages of the disorder. With this unique vantage point, they can gather data on key genetic, physiologic, and psychological variables involved in TMJMD pain, ultimately weaving the information into more effective treatments.

Only a decade ago, a large study tracking the development of TMJMD over time would have been scientifically problematic, because little was known about the basic mechanisms of human pain. However, because progress in the basic sciences has fed the knowledge pipeline, pain researchers have now better defined the molecular circuitry involved in pain transmission, thereby providing the conceptual framework for this important clinical study.

MOLECULAR MEDICINE AND ORAL CANCER

In the fight against cancer, future weapons of choice likely will fall within the therapeutic category of molecular medicine. The concept builds on world-wide efforts to design cancer treatments targeting the precise molecules that drive the tumor process, leaving normal cells unscathed. As envisioned, molecular medicine will increase the benefits of treatment and limit greatly the unwanted side effects that now afflict cancer patients. For the vision to become reality, scientists first must learn to correctly identify distinctive features of the genetic and/or protein profiles of developing tumors. Much progress has been made in the laboratory, but the

¹Martin JA, Hamilton BE, *et al.* Births: Final data for 2003. National vital statistics reports; vol. 54 no 2. Hyattsville, MD: National Center for Health Statistics. 2005.

²Offenbacher S, Katz V, *et al.* Periodontal infection as a possible risk factor for preterm low birth weight. *J Periodontol*, vol. 67(10) p. 1103–13.

promise of molecular diagnostics remains largely unready for translation to patient care.

An NIDCR-supported project that has successfully taken that critical step is a partnership between scientists, dental educators, and a community clinic in British Columbia. The partners have integrated molecular techniques with existing screening tools by combining certain molecular discoveries with clinical use of toluidine blue, a chemical dye used to determine whether or not to biopsy an abnormal growth. The technique hinges on laboratory work that showed an association in early oral lesions between toluidine blue retention and the presence of cells with distinct, cancer-predisposing chromosomal abnormalities. The program already has identified several people requiring treatment for oral cancer and pre-cancerous lesions.

DRY MOUTH AND RADIATION THERAPY

Persistent dry mouth often occurs in head and neck cancer patients because radiation from the therapy damages the salivary glands. This irreversible, chronic dryness makes normal chewing and swallowing difficult, and leads to a range of painful oral diseases. Recently, NIDCR scientists teamed with researchers at the National Cancer Institute to develop an important new lead in protecting the salivary glands during radiation therapy to the head and neck. Their work involves a synthetic chemical called Tempol, which possesses a unique ability to protect cells against radiation. In mice, administration of Tempol 10 minutes prior to radiation therapy to the head and neck provided significant protection to the salivary glands. Critically, Tempol did not protect tumors from radiation, and thus did not diminish the beneficial effects of the radiation therapy. Future clinical trials in people are likely.

REDUCING DISPARITIES IN THE NATION'S ORAL HEALTH

Although the Nation's oral health has improved greatly over the past several decades, this progress has not been equally shared by millions of low income and underserved Americans. To help reverse this trend, the NIDCR supports five Centers for Research to Reduce Oral Health Disparities. The centers are designed to explore, understand, and improve the oral health of those who reside in underserved communities. The researchers seek creative but practical approaches that are inexpensive, can be easily applied, and are exportable to other underserved communities.

This year, the Disparities Centers reported several noteworthy findings. For example, after a two-year clinical study, San Francisco researchers found that infants and small children who receive at least one fluoride varnish treatment per year can cut their dental caries rate in half. Fluoride varnish is a concentrated fluoride in a resin or synthetic base that is applied directly onto the teeth. The treatment is inexpensive and is more easily used with very small children than other preventive measures, such as dental sealants and mouth rinses.

Meanwhile, the Disparities Center at the University of Washington is evaluating the oral health benefits of gum and candy sweetened with xylitol rather than caries-promoting sugars. Xylitol, a natural substance found in certain fruits, has been shown to fight tooth decay. The team is refining the optimal dose to satisfy taste and fight decay. Xylitol use exemplifies an easily adopted, self-administered, scientifically validated approach that may be useful in underserved populations.

IMPROVING THE NATION'S ORAL HEALTH

As these highlights demonstrate, the NIDCR has made a strong commitment to expand clinical research and to build the evidence base that will inform better clinical practice. At the same time, progress in basic science continues to provide new and exciting leads that can translate into large clinical trials, yielding results with the potential to transform dentistry and public health. Above all, the NIDCR seeks to find practical solutions to intractable problems and, in so doing, improve the Nation's oral health.

PREPARED STATEMENT OF DR. NORA VOLKOW, DIRECTOR, NATIONAL INSTITUTE ON DRUG ABUSE

Mr. Chairman and Members of the Committee: I am pleased to present the fiscal year 2007 President's budget request for the National Institute on Drug Abuse (NIDA). The fiscal year 2007 budget estimate is \$994,829,000, a decrease of \$5,200,000 from the fiscal year 2006 enacted level of \$1,000,029,000, comparable for transfers proposed in the President's request.

INTRODUCTION

The National Institute on Drug Abuse, within the National Institutes of Health (NIH), is once again pleased to report continuing declines in overall drug use among our Nation's youth. NIDA has focused much of its research on the vulnerable adolescent period of development, since this is when drug abuse typically takes hold and can bend a young life toward long-term drug abuse problems or addiction. Research findings elucidating the mechanisms of action and destructive consequences of drugs of abuse on the brain and body appear to be getting through to this population. For example, the 2005 Monitoring the Future (MTF) Survey of 8th, 10th, and 12th graders shows a dramatic 19 percent reduction in use since 2001. However, areas of significant concern remain, including the alarmingly high rates of non-medical use of painkillers among 12th graders, the high rates of stimulant abuse among 12th graders, and the spread of methamphetamine abuse to new geographic areas of the country.

Therefore, while we can acknowledge and appreciate the positive effects of evidence-based prevention and treatment efforts, we also recognize the need to keep pace with emergent problems. To this end, ongoing support of leading edge research by NIDA scientists continues to enhance innovative prevention and treatment interventions, while collaborations with other Institutes and public and private partners make optimal use of our research infrastructure.

PRESCRIPTION DRUG ABUSE—THE PROBLEM WITH PAINKILLERS

According to the 2004 National Survey on Drug Use and Health, nearly three-fourths of the estimated 6 million people aged 12 and older who reported non-medical use of prescription psychoactive drugs said they abuse pain relievers in particular, with young adults (18–25) showing the greatest increases in lifetime use from 2002–2004. Even younger populations are involved, revealed by findings from NIDA's 2005 MTF Survey.

NIDA is tackling this growing problem from multiple angles, seeking to understand the factors that have brought us to this point so that we may reverse negative trends and stop new ones from emerging. Underlying factors include the fact that opioids are now among the most commonly prescribed medications, that society is more accepting of using medications to treat all kinds of health problems, and that the Internet provides greater access to prescription drugs.

In response to these concerns, NIDA's new initiative on prescription opioids and treatment of pain is soliciting a broad range of preclinical and clinical studies from across the sciences. We will examine the basic mechanisms involved in pain and how their interaction with prescription painkillers influences addiction potential—for example, whether opiates are equally addictive to an individual in pain versus one who is not in pain. Research on the basic interactions between pain and opioid systems is needed to inform physicians about associated abuse risks and to guide their prescribing practices.

Other strategies for reducing prescription painkiller abuse include developing alternative pain medications and promoting better delivery systems for painkillers to minimize abuse potential. Recent studies have identified a subset of cannabinoid receptors (i.e., CB2 receptors) as promising new targets for treating chronic pain from nervous system injury. In addition, because of their lack of activity in brain reward centers and diminished abuse liability, novel CB2-based medications present an attractive alternative for treating chronic pain. Buprenorphine/naloxone, a recently approved medication for the treatment of opioid addiction, represents another approach. Acting on the same brain receptors as drugs like heroin and morphine, buprenorphine does not produce the same high, physical dependence, harsh withdrawal symptoms, or dangerous side effects. Further, its unique formulation with naloxone, an opioid antagonist, produces severe withdrawal symptoms in addicts who inject it to get high, thereby lessening the likelihood of diversion while maintaining desired therapeutic properties. NIDA is planning a multiple trial study to evaluate the effectiveness of buprenorphine in the treatment of the pain patient who is addicted to his/her pain medication and to help develop guidelines on how to treat these types of patients.

GENES, ENVIRONMENT, AND BEHAVIOR

A person's individual genome, or genetic makeup, plays an important role in determining his or her vulnerability to or protection against addiction. Studies of heredity have shown that about 40–60 percent of predisposition to substance abuse can be attributed to genetics, with environment impacting how those genes function or are expressed. Addiction is a quintessential gene-x-environment interaction dis-

ease: that is, a person must be exposed to drugs (environment) to become addicted, yet exposure alone is not determinative—genes interact with this environment to create a vulnerability to addiction. Growing knowledge about the dynamic interactions of genes with the environment confirm addiction as a complex and chronic disease of the brain with many contributors to its expression in individuals.

NIDA is studying these interactions to see what they reveal about vulnerability to addiction and to other adverse effects of abused drugs. For example, one recent study found that carriers of a common variant of the COMT gene were more likely to exhibit psychotic symptoms and to develop schizophreniform disorder if they used marijuana.

Thus, people with particular genes may suffer more harmful effects from drugs of abuse.

To expedite the translation of findings that could help identify the location of genes that confer vulnerability or protection, NIDA is supporting innovative research to help design, develop, and market technology to conduct rapid behavioral throughput screens for identifying genetic vulnerability using animal models of drug abuse and addiction. This information could then become part of a database of candidate genes for drug abuse, for eventual mapping and for targeted therapeutic application. Advances in genetics research in addiction are already suggesting ways to tailor our interventions to have the greatest impact. For example, a recent study showed that distinct alleles of the dopamine receptor gene led to different outcomes according to the type of smoking cessation therapy used—bupropion or nicotine replacement therapy. Such findings provide a glimpse of a future in which a patient's genetic background will be a major factor in selecting the most appropriate therapeutic course of action.

Other NIDA studies are also helping to unravel the ways in which environmental factors, such as stress, induce brain changes that interact with drugs of abuse and alter behavior. It is well known that stress is a major cause of relapse to drug abuse in recovering addicts and can prompt the release of a neurochemical, corticotrophin releasing factor (CRF). Recent research showed that in cocaine-exposed animals, stress-induced CRF triggered drug-seeking behavior, even as long as 3 weeks after exposure. This research highlights the concept of persistent brain changes leaving individuals vulnerable to certain relapse triggers like stress. Moreover, stress may be common to a variety of conditions, including depression, anxiety, and some forms of overeating and obesity. By revealing the precise brain mechanisms involved in stress, our research can lead to treatments that for these conditions.

We are also learning how environmental factors not only alter the expression but the structure of genes involved in brain function, which then influences an individual's behavior. Known as "epigenetics," this field gives researchers an opportunity to investigate gene-environment interactions, including the deleterious changes to brain circuits resulting from drug abuse. Understanding how drugs of abuse effect epigenetic changes may help in developing interventions to counter or prevent such changes. A recent study of demonstrated that cocaine caused significant structural changes to the DNA in regions containing genes implicated in shaping the brain's response to drugs of abuse; furthermore, in animals genetically engineered to minimize those changes, the rewarding effects of cocaine were dramatically reduced. These results show how gene-environment interactions can change the brain and drive behaviors associated with drug addiction. NIDA is supporting innovative research to help design, develop, and market technology to conduct rapid behavioral throughput screens for identifying gene/environment interactions.

SOCIAL NEUROSCIENCE

NIDA is targeting the influence of social factors both in individual and group decision-making. This focus is critical not just to understanding drugs of abuse but other health behaviors as well. For instance, a social neurobiological perspective is being applied in NIDA studies investigating the mechanisms underlying adolescents' increased sensitivity to social influences (i.e., peers) and decreased sensitivity to negative consequences of their behavior that together make them particularly vulnerable to drug abuse.

A recent NIDA request for research in the emerging field of social neuroscience is soliciting studies from basic to clinical science as we work to examine how neurobiology and the social environment interact in abuse and addiction processes (e.g., initiation, maintenance, relapse, and treatment). We now have the tools to see how genetics, epigenetics, and brain chemistry can change social behavior and how the social interactions of an individual can change his or her brain. For example, studies of early maternal behavior in animals demonstrated that offspring receiving low levels of care during their first week of life developed an over-responsive stress

system that lasted a lifetime. In this case, genes responsible for regulating stress responses were “silenced” by environmental manipulation. Some of these changes can be reversed in adulthood by targeted intervention, making this research area ripe for developing approaches to counteract the effects of adverse environmental impacts, which in the case of stress are known to increase the risks for substance abuse.

We are also committed to efforts to better characterize “phenotypes” of social environments and to understand their interaction with other vulnerabilities, such as genetics. One approach could include strategies such as mapping community risk factors for drug use (e.g., parental practices, family structure, school systems, socio-economic status, neighborhood characteristics, and drug availability) and to use that knowledge to inform us about mediators of the social stressors that elevate risk for drug abuse. A better understanding of this relationship is relevant both for the treatment of drug addiction and for psychotherapeutic interventions for mental illnesses, which also involve social aspects of human behavior.

DRUG ADDICTION TREATMENT WORKS

NIDA’s research findings have demonstrated that drug addiction treatment works. Moreover, comprehensive treatments (i.e., those that include a combination of available medications, behavioral treatments, and job training and referral services) tailored to the needs of the individual patient have the highest success rates. We continue to work with the private sector to develop medications to use with behavioral therapies to treat drug addiction, and are pursuing collaborations with pharmaceutical companies to move novel and promising compounds forward to clinical evaluation. In addition, NIDA’s initiative focusing on pilot clinical trials of new addiction medications will invigorate the field by helping investigators generate sufficient safety and efficacy data to support full-scale clinical trials and expedite the possible progression of novel medications to real-world use.

Over the past year, we have made great progress in identifying potential medications for treating drug addiction, including addiction to stimulants such as cocaine and methamphetamine. Several promising compounds have been identified in animal studies, and initial clinical efficacy for drug abuse has been demonstrated for medications marketed for other uses: disulfiram, prescribed for alcoholism; modafinil, for treatment of narcolepsy; and gamma-vinyl GABA (not marketed in the United States) and topiramate, both used to treat seizure disorders. Progress is also being made in the area of vaccine development for cocaine and nicotine addiction, and Rimonabant, a cannabinoid receptor blocker is a promising candidate for treating marijuana addiction. Close to being approved for marketing by the pharmaceutical industry as a weight loss aid, Rimonabant may also have the potential to prevent relapse to cocaine, heroin, and methamphetamine abuse, and nicotine addiction. Marinol, another cannabinoid receptor agonist, may also show promise as a treatment for marijuana withdrawal symptoms.

Interventions are also needed to treat comorbid mental disorders and addiction. For example, given that an estimated 15–30 percent of patients with substance abuse problems also suffer from comorbid ADHD, as found in research studies, NIDA has launched a large clinical study in our Clinical Trials Network (CTN) to test whether treatment of ADHD with methylphenidate, in parallel with treatment for substance abuse, will improve outcomes in those who suffer from both conditions.

We are also developing drug abuse treatments for use in the criminal justice system. Our research findings show that drug treatment works even for people who enter it under legal mandate, with outcomes as favorable as for those who enter treatment voluntarily. To illustrate, in a Delaware Work Release study sponsored by NIDA, those who participated in prison-based treatment followed by aftercare were seven times more likely to be free of drugs after 3 years than those who received no treatment. Moreover, nearly 70 percent of those in the comprehensive drug treatment group remained arrest-free after 3 years—compared to only 30 percent in the no-treatment group. We are helping to integrate drug treatment into the criminal justice system and improve outcomes for offenders through our comprehensive Criminal Justice Drug Abuse Treatment Studies (CJ-DATS) initiative, undertaken in collaboration with Federal, state, and local criminal justice partners.

NIDA research has demonstrated the value of drug addiction treatment programs in helping patients recover from the complex disease of addiction. Faith-based and community-centered programs are often part of long-term recovery, yet their effectiveness and role in delivering treatment needs to be studied more extensively. NIDA is conducting research to examine this role.

HIV/AIDS AND MINORITY DISPARITIES

The latest data from the Centers for Disease Control and Prevention (CDC) suggest that the HIV/AIDS epidemic is evolving, with drug abuse still a major vector in its spread. Progress in treating injection drug abuse has helped to decrease HIV transmission among this highly vulnerable population, influenced by a multi-pronged approach including community-based outreach to reduce risky behaviors and development of medications such as methadone and buprenorphine to treat injecting drug users. But while this approach has helped reduce U.S. cases from this route of transmission, other countries, such as Russia and Southeast Asia, continue to report that injection drug abuse accounts for a large proportion of their HIV/AIDS cases. Thus NIDA is supporting international studies to promote HIV prevention practices and use of medications to treat drug addiction. Depot-Naltrexone is one such possibility, since it is a long-acting opioid antagonist medication expected to soon receive approval for treatment of alcohol addiction. Because efforts to decrease drug abuse also modify the behaviors that can lead to HIV transmission, we believe strongly that drug abuse treatment is HIV prevention.

Early detection of HIV helps prevent HIV transmission and increase health and longevity. NIDA-supported research indicates that routine HIV screening, even among populations with prevalence rates as low as 1 percent, is as cost effective as screening for other conditions such as breast cancer and high blood pressure. These findings have important public health implications, but require efforts to increase HIV screening acceptability (similar to mammography) in order to be effective.

We are also deeply concerned about the disproportionate impact of HIV/AIDS on African Americans. For while they represent just 13 percent of the U.S. population, African Americans account for 42 percent of AIDS cases diagnosed since the start of the epidemic, according to CDC. In fact, data from the CDC's National Vital Statistics Report published in 2003 show that HIV/AIDS is the leading cause of death among all African Americans 25–44 years old, ahead of heart disease, accidents, cancer, and homicide.

To address these disparities, NIDA is encouraging research on the nexus of drug abuse and HIV/AIDS among African Americans to understand the risk factors and the pathways between them and to develop culturally sensitive prevention and treatment programs for drug abuse and HIV/AIDS. We are committed to making sure this research is translated in a meaningful way.

FROM BENCH TO BEDSIDE TO COMMUNITY

NIDA is proud of our myriad efforts to translate the results of our basic and clinical research on the brain and body effects, getting new treatments into the hands of providers who will use them, disseminating prevention messages to people who will hear them, and raising the awareness of people who can help change the course of drug abuse treatment in this country. Our audiences are many and include physicians, teens, teachers, judges, parents, and others.

Through our physician outreach initiative, we are funding efforts to develop strategies for primary care physicians to better identify and serve drug abusing patients through use of science-based screening and brief interventions. We are also supporting development of a pilot judicial training curriculum in Cook County, Illinois, to help criminal court judges understand the neurobiology of addiction and the effectiveness of treatment. The goal of this program is to better inform judicial decision-making with regard to substance-abusing offenders. These efforts will be applied to the Federal court system as well. We also support grants to evaluate results from drug courts to achieve optimal dissemination and improve outcomes, and we will soon publish a book of treatment principles for application with individuals involved in the criminal justice system.

Our education portfolio continues to grow and includes a wealth of materials, such as our NIDA Goes Back to School Initiative, a science education campaign to provide middle school students with information about how drugs work in the brain. An interactive website complements this effort, allowing students and teachers to easily obtain additional information about drugs of abuse. To help young people understand the risks of drug abuse leading to HIV infection, NIDA and our partnering organizations—including the American Academy of Child and Adolescent Psychiatry, the AIDS Alliance for Children, Youth, and Families, and the United Negro College Fund Special Programs Corporation—recently launched a multimedia educational campaign, including a public service announcement and website, to help young people “learn the link” between drug abuse and HIV infection. We are translating these materials into Spanish and making them culturally relevant for different populations.

We are also collaborating with our sister agency, the Substance Abuse and Mental Health Services Administration (SAMHSA) and with the National Institute of Mental Health on a new initiative to enhance the capacity of community-based providers of drug abuse treatment services. We continue to work with SAMHSA, supporting the development and dissemination of research-based products through their Addiction Technology Transfer Centers across the country, applying findings from our Clinical Trials Network and other research. And because addictive, psychiatric, and neurological disorders emerge from common neural substrates, a tremendous amount of inter-Institute collaboration has taken place—an approach we will continue to emphasize, given its ability to produce sharable findings and cost efficiencies.

CONCLUSION

Our investment in basic and clinical research has changed the way people view drug abuse and addiction in this country. We now know how drugs work in the brain, their health consequences, how to treat people already addicted, and what constitutes effective prevention strategies. As science advances, NIDA's comprehensive research portfolio is strategically positioned to capitalize on new opportunities. We continue to make great strides in translating and disseminating the products of our research, so they can be used in real communities by people who need them, providing front-line clinicians around the country with the tools needed to reduce drug abuse and addiction in our Nation. To make the most of scarce resources, we depend on a rigorous planning and priority-setting process that not only supports our strong commitment to reducing drug abuse and HIV transmission in this country, but extends to other health fields represented by NIH. Sustaining the momentum of our efforts will lead to even more discoveries that will improve the health and safety of all Americans.

Thank you, Mr. Chairman. I will be pleased to answer any questions the Committee may have.

IMPACT OF BUDGET CUTS

Senator SPECTER. We will now proceed with questioning by the Senators, 5 minutes each.

Dr. Zerhouni, you say you will continue to deliver. How is that possible when you have had more than a 10 percent decrease, considering inflation, which amounts to about \$3 billion? The comments that I hear relate to there being a panic, panic among the applicants for NIH research. How can you continue to deliver with that kind of a budget?

Dr. ZERHOUNI. It is very important to realize that medical research cannot be funded through ups and down. We have to sustain the investment over time, and it is clear that medical research requires support for scientists. What is happening right now is that through the doubling we have generated a new generation of scientists. We have over a 50 percent increase in the number of scientists.

Senator SPECTER. What is the consequence of the cut?

Dr. ZERHOUNI. The consequence of the cut is very simple. If you keep investing below and lose purchasing power, the most important impact on research is loss of scientists. This is what we have seen in the past and this is what may happen again if we do not sustain our investment in medical research.

PREPAREDNESS FOR PANDEMIC INFLUENZA

Senator SPECTER. Dr. Fauci, there is a great concern, as we all know, about pandemic influenza. This subcommittee has held a series of hearings on the subject. How are we doing? What are the prospects for being prepared if that wave should strike us in the United States?

Dr. FAUCI. From the standpoint of the scientific preparation for developing vaccines and drugs, from the last time I testified before you, Mr. Chairman, which was just a couple of months ago, we have made even more progress. We have, as you know, as Dr. Zerhouni alluded to, we have a vaccine that is currently in clinical trial in different age groups and demographic groups. We have tested it and published the results in healthy young adults. We have tested it in the elderly and in children. As I mentioned to you at the last hearing, the vaccine appears to be very well tolerated and induces an immune response that would be predictive of being protective.

There is a big problem with it, though. The problem relates to the fact that the dose that is required to induce the level of immunity that you would predict would be protective is prohibitively high, which is leading us to the studies that are ongoing now, namely the use of what we call adjuvants, or compounds which expand the capability of the immune system to respond. Those studies are ongoing right now.

FUNDING FOR PANDEMIC INFLUENZA

Senator SPECTER. Is the funding adequate?

Dr. FAUCI. We could do more with more funding, there is no doubt about that. I would be——

Senator SPECTER. How much do you need?

Dr. FAUCI. It is difficult to put a number on it, except to say that——

Senator SPECTER. Well, if you cannot put a number on it, we cannot.

Dr. FAUCI. Well, we need—for example, if I could bring one component up that I think would be of interest to this committee, is that we are currently pursuing rather aggressively the concept of what we call a universal influenza vaccine, namely a vaccine that cross-reacts from season to season and would also be protective against the pandemic flu.

Senator SPECTER. Dr. Fauci, I am reluctant to cut off a witness with your distinctive record. Give us in writing what funding you need.

Dr. FAUCI. Okay, I could do that for you.

[The information follows:]

FUNDING FOR PANDEMIC INFLUENZA

The National Institute of Allergy and Infectious Diseases (NIAID) supports a robust and diverse portfolio of research on influenza, including pandemic influenza. Many opportunities to accelerate the research and development of medical countermeasures against influenza as well as to advance our understanding of influenza viruses could be pursued in fiscal year 2007 and fiscal year 2008 should additional funds become available. In its professional judgment that is outside the context of other competing priorities, NIAID estimates that it could obligate an additional \$212 million in influenza research in fiscal year 2007 above the budget request and an additional \$458 million in fiscal year 2008.

NIAID could use such funds to accelerate research and development of antiviral drugs, vaccines, adjuvants, and diagnostics for influenza. For example, NIAID could accelerate the development and clinical testing of promising universal vaccine candidates, which could offer protection against multiple influenza virus strains, and the development of new and improved vaccine strategies for influenza such as recombinant subunit vaccines and gene-based vaccines that may allow for more rapid production of a vaccine against a pandemic strain of influenza, should one emerge.

These additional funds also could facilitate the expansion of critical research resources, such as animal models and clinical trials infrastructure that are essential for the development of medical countermeasures against influenza.

Underpinning efforts to develop medical interventions against pandemic influenza is research into the basic biology and disease-causing mechanisms of influenza viruses. With additional funding, NIAID could expand basic research in the areas of influenza virology, pathogenesis, epidemiology, immunology, genomics, proteomics, and systems biology as well as to expand international animal surveillance activities. This research is crucial to the development of antiviral drugs, vaccines, and diagnostics for influenza.

CANCER GENOME ATLAS

Senator SPECTER. Let me turn now to Dr. Niederhuber with respect to the cancer-genomics initiative. Can that be implemented with the current funding? What do we need to successfully prosecute the war against cancer?

Dr. NIEDERHUBER. Well, Senator Specter, thank you. We are very committed, the National Cancer Institute, with our partner, the National Human Genome Research Institute, to initiate a pilot project on the Cancer Genome Atlas. Each Institute has committed \$50 million from our existing resources to do that. This will be a pilot project which is helping us understand the technology needs, the technology advancements, and our ability to do this project.

Senator SPECTER. Dr. Niederhuber, would you supplement your testimony today with a memorandum as to what you need as to that program and as to the war on cancer overall?

Dr. NIEDERHUBER. Absolutely, sir.

Senator SPECTER. Give us a winning strategy for that war?

Dr. NIEDERHUBER. Absolutely.

[The information follows:]

CANCER GENOME ATLAS

The Cancer Genome Atlas program is the product of several years of investment by the NCI in the Cancer Genome Anatomy Project (C-GAP) and other large scale genomics programs, some of which were performed in collaboration with the NHGRI. These efforts culminated in 2003 with a report from the NCI's National Cancer Advisory Board (NCAB) which recommended that the two Institutes undertake a pilot program to determine the feasibility of systematically developing an "atlas" of all genetic alterations involved in cancer.

Active planning for The Cancer Genome Atlas, or TCGA, began in the latter half of 2002 as a consequence of progress and convergence of science and advanced technologies in three distinct areas. First, the completion of the sequencing of the human genome provided for the first time in history a benchmark to begin to understand the effect of genetic changes on the etiology and progression of diseases such as cancer. Second, our years of investment in understanding cancer at the molecular level resulted in the discovery of some very important genetic changes in cancer cells that led to the development of targeted drugs such as Gleevec and Herceptin. Based on an understanding of the specific genetic alterations driving specific tumors, these targeted drugs allowed oncologists for the first time to target specific genetic alterations in patients with chronic myelogenous leukemia (CML) and breast cancer, respectively. Finally, the pace of technology development in analyzing all aspects of genes and their products is accelerating—setting the stage for large scale interrogation of the genome to understand the role of genetic mutation in diseases such as cancer. Interestingly, one of the major requirements for this project is the development of an unprecedented data management system and ultimately an accompanying database; NCI's investment in the Cancer Bioinformatics Grid (caBIG) over the past several years provides the advanced technology platform needed to meet this need.

Cancer is a disease of changes in genes that occur over an individual's lifetime. Three kinds of genetic alterations contribute to cancer—those that occur in the DNA of egg or sperm and are passed from a parent to offspring (germline mutations),

those that occur as a result of exposure to the environment (somatic mutations) and changes in DNA that lead to changes in genes that control proteins involved in transcription and translation. Additionally, changes in gene function can occur without a change in the sequence of DNA (epigenetic changes). TCGA will finally facilitate an in-depth understanding of how these types of genetic changes differ in terms of their role in an individual's inherited risk vs. those changes that arise from environmental exposure. It is the latter category of mutations that will allow scientists to obtain a clear picture of the impact of these somatic mutations on the major pathways that appear to drive many of the major hallmarks of cancer cells. Overall, the TCGA pilot project, much like the Human Genome Project, has the potential to create an unparalleled knowledge base, drive a new era of discovery by scientists from all fields of biomedical research and ultimately provide a new paradigm for the prevention, detection and treatment of chronic diseases such as cancer.

The NCI and NHGRI believe strongly that TCGA is one of the most important projects undertaken in medicine to date. It leverages all that has gone before and for the first time will allow scientists to apply our understanding of the human genome sequence to cancer—a disease that will strike over 1.4 million Americans this year and kill over 560,000 at a cost of well over \$190 billion. We are committed to getting this project underway within current budget constraints. The NCI has identified funds for redeployment from other projects, and the NHGRI will dedicate a large portion of its sequencing capacity to performing this first-ever large scale effort in medical sequencing.

The information generated by the TCGA pilot project will provide the necessary scientific data by which the Institutes and the scientific community can evaluate the preliminary outcomes of the research.

The convergence of our understanding of cancer at the molecular level, advanced genome analysis technologies, especially bioinformatics, and experience gained in the Human Genome Project, allow us to now undertake TCGA, a project that promises to contribute significantly to the development of 21st century medicine. Both the NCI and the NHGRI are committed to leveraging these strengths to ensure that we move forward toward our goal of personalized medicine for cancer and all diseases.

A WINNING STRATEGY AGAINST CANCER

NCI has developed a Strategic Plan to reduce and eliminate the suffering and death due to cancer with the help of the scientific community. The Plan sets forth a framework within which NCI can use its funding, infrastructure, tools, and intellectual resources to lead and work with others. We set forth eight strategic objectives in the Plan and these will be instrumental in guiding our operational level plans and serve as an organizer for measuring and reporting progress. A complete description of the Strategic Plan can be found on NCI's web site at <http://www.cancer.gov/aboutnci/2015>.

There are two basic tactics—preempting cancer and ensuring the best outcomes for all—embodied in the Plan's objectives.

To preempt cancer at every opportunity, there are four strategic objectives:

- Understand the causes and mechanisms of cancer;
- Accelerate progress in cancer prevention;
- Improve early detection and diagnosis; and
- Develop effective and efficient treatments.

To ensure the best outcomes for all, there are four strategic objectives:

- Understand the factors that influence cancer outcomes;
- Improve the quality of cancer care;
- Improve the quality of life for cancer patients, survivors, and their families; and
- Overcome cancer health disparities.

To achieve these objectives requires numerous funding vehicles and support mechanisms throughout the cancer research community. The steps we could take in order to accelerate progress to eliminate the suffering and death due to cancer include:

- Rapid development of an integrated technology initiative;
- Deployment of a modern integrated clinical trials infrastructure;
- Expansion and integration of the Cancer Centers program; and
- Mechanisms and Flexibilities—streamlined procurement and review processes to acquire materials and services and coordination of licensing and patenting activities.

An integrated advanced technology initiative for cancer could provide a linkage between the National Cancer Program and R&D initiatives being developed in selected national laboratories and advanced technology facilities located in more than 40 states and regions. Connected in real-time through a common bioinformatics

grid, forming a “network of networks” of science, technology, and treatment, such an initiative could serve to accelerate the emerging discipline of molecular oncology. This would create a pipeline of new personalized cancer diagnostics and therapeutics from bench concept to bedside and community delivery. In the next few years, such an initiative could:

- Accelerate the implementation of a nationwide high-end information technology grid for bioinformatics that could be uniquely adapted for real-time data sharing. NCI’s pilot version, called caBIG, is slated for full-scale implementation this year and, during the pilot phase, was implemented among 50 Cancer Centers, FDA, and other organizations.
- Develop a comprehensive biomarker discovery and validation program.
- Foster the application of emerging technologies, such as nanotechnology, and integrate molecular agents with advanced imaging devices.
- Accelerate a nationwide real-time medical information electronic system for research and medical data sharing using technologies and devices currently employed by the banking industry and large-scale commercial enterprises.
- Enhance the discovery and validation of new targets of genes and proteins critical to cancer development.

NCI could deploy a more modern and integrated infrastructure for cancer clinical trials. This clinical research infrastructure could:

- Strengthen collaborations with industry, FDA, Centers for Medicare and Medicaid Services, and other public, private, academic, and patient advocacy organizations to oversee the conduct of cancer clinical trials.
- Develop new infrastructure and procedures to standardize, coordinate, and track clinical trials development and accrual across all NCI-supported clinical trials.
- Increase utilization of imaging tools in screening and therapy trials, evaluate new imaging probes and methodologies, enable access to the imaging data from trials in an electronic format, and facilitate evaluation of image-guided interventions.
- Expand access and improve the timeliness for completion of the highest priority clinical studies.
- Foster the development of a cadre of established clinical investigators who could work between bench and bedside.
- Pilot new approaches and develop prototypes for clinical trials networks that could improve the efficiency, coordination, and integration of our national efforts.
- Develop a common clinical trials informatics platform that could be made available to the full range of investigators working within the cancer clinical trials system.

NCI plans to accelerate the expansion and integration of the NCI-designated Cancer Centers program, including the addition of 14 new Cancer Centers, increasing the number of centers to 75. The Cancer Centers program could:

- Implement progressive bioinformatics and communication systems to achieve horizontal integration.
- Fund additive programs in collaborative, multidisciplinary research, and require integration and sharing of results.
- Broaden the geographic impact of the centers, networks, and consortia and vertically integrate them with community and regional health care delivery systems.
- Improve the access of minority and underserved populations to state-of-the-art research and resources.
- Create and strengthen partnerships with government agencies and community organizations.
- Broadly provide expertise and other resources to caregivers, patients and families, and appropriate health agencies.

In addition to appropriations, flexible legislative authorities related to exemptions from specific parts of current procurement, grant review and processing, and licensing and patenting rules could also help accelerate progress. A streamlined procurement process could facilitate the acquisition of materials and services to support the R&D activities. Technology development could also be enhanced by sufficient flexibility and integration to enable interactions among a wide array of laboratories and other entities. Expedited review procedures and workflow processing could help to award funds in sequence as needed. Coordination of the licensing and patenting activities among grantees, contractors, and the intramural program could also be useful for many of the multicomponent technology platforms that could be created through an advanced technology effort.

WOMEN'S HEART DISEASE

Senator SPECTER. Let me turn now to Dr. Nabel. What have the results been with the Women's Health Study? With respect to heart disease, we know that women are affected differently. I want the record to note that my question ends with no red light, but you can proceed.

Dr. NABEL. Thank you, Mr. Chairman.

The women's health initiative was an important study conducted over 15 years with 161,000 women in this country ages 50 to 79 participating. We gathered important information about heart disease, the number one killer of women in this country.

From other studies, we realize that heart disease often manifests itself in women differently than men. We have come to recognize what those symptoms are. We have come to recognize that some of the diagnostic tests have to be different and we have come to recognize that some of the treatments have to be specifically focused towards women.

These studies have given us a tremendous amount of information. We now have engaged in a very large public awareness education campaign and we are in the midst of helping women to understand what their risks are for heart disease and how to seek help when they need it.

Senator SPECTER. Thank you.

Senator Harkin.

NATIONAL CHILDREN'S STUDY

Senator HARKIN. Thank you, Mr. Chairman.

Dr. Zerhouni, of all the proposed cuts in the budget there is one that I think may be discouraging than all the rest, and that is the planned elimination of the National Children's Study. We passed this legislation back in 2000. It was going to be the largest long-term study of children's health ever conducted in the United States. It was going to involve 100,000 children from before birth to adulthood. The idea was to better understand the link between the environments where the children are raised and their physical and emotional health and development.

We have already spent about \$50 million planning the study, 4 to 5 years of planning on it. Now I understand that the study is going to stop. Why is that?

Dr. ZERHOUNI. Well, the study has had a pilot phase to evaluate feasibility. The issue really is, you are talking about a very long study with a large budgetary impact, and at the end it was just a matter of budgetary priorities which led to the decision of not completing the pilots at this time, but to look at other times when the budgets will be easier.

Senator HARKIN. I understand that the budgetary impact was \$70 million. Is that correct or not?

Dr. ZERHOUNI. If you look at—the \$70 million is not just a 1-year expenditure. In fact, you have to continue that expenditure. If you committed to that expenditure, Senator, then you have committed to the \$3.2 billion or thereabouts total over the total study. Why? Because once you launch the study you have to continue recruitment of the 100,000 children, the parents, and so on.

So if you look on the screen that tries to describe the evolution, it is \$69 million in 2007, \$111 million in 2008, \$192 million, \$194 million, and so on. So this is what led to the budgetary conclusion for these tight fiscal times. Committing to 2007 meant not just 2007, but a whole series of budgetary commitments, and in the context of projections it was very hard to see how it would fit in.

WOMEN'S HEALTH INITIATIVE

Senator HARKIN. Well, as you know, it was supposed to start by the end of this fiscal year.

Dr. Nabel, how long was the women's health initiative study?

Dr. NABEL. 15 years, Mr. Senator.

Senator HARKIN. 15 years.

Dr. NABEL. Yes.

Senator HARKIN. Obviously, we got a lot of good information out of it.

Dr. NABEL. We sure did.

Senator HARKIN. What did that cost, do you know?

Dr. NABEL. In total, about \$710 million.

Senator HARKIN. For the 15 years. How many women did it cover?

Dr. NABEL. 161,000 women.

Senator HARKIN. This is 100,000 children and it was supposed to be how many years study? About 20—

Dr. ZERHOUNI. 21 plus 4, so about 25 years, and about \$3.2 billion is the number I remember, but upwards of that.

Senator HARKIN. Well, it seems to me from the women's health initiative we learned the benefits of long-term studies, long-term longitudinal studies. It seems to me with everything that is impacting on obesity, to diabetes to mental health, kids and how they grow up, there is just a lot of things that need to be taken into account. If you do these studies, then you would be able to factor some of these things in after a longer period of time.

I just find this very disturbing that we are cutting this program. I am hopeful that we can put this back in the budget. Maybe this is another result of the President's budget. I do not know. Is that what it is? I am just asking it rhetorically. I do not expect an answer, but I am just asking this rhetorically. If that is what it is, then we have got to find the money to put back in there.

This did not just come up. This is something that we had talked about for a long time with your predecessor and others, about getting this very long-term study done. We just assumed, at least I did anyway, that it was on track and that we were going to do it, and all of a sudden this year it pops up and it is going to be eliminated. EPA was coming in on the study, I think, also CDC was also going to partner in the study, if I am not mistaken.

Dr. ZERHOUNI. No, you are not mistaken, Senator. It was a trans-governmental study. It was not just an NIH study. It really involved 14 different departments. Environmental health was important, genetic health was important. Education was involved as well. So 14 Federal agencies were involved.

Senator HARKIN. Well, I am just wondering what kind of a priority would this be in the scheme of things. Is this just something

that we can just drop out the bottom, or is this really an important study to be done? Is it important or not?

Dr. ZERHOUNI. So the issue is really an issue of prioritization, and you have a pilot phase study so we can evaluate whether or not to go forward. But you mentioned yourself the critical factor of sustaining success rates, and so in the context of those decisions you can see where, in a constant sum budget, studies like this will have a large impact on success rates across the board. Therefore, when you look at the investments that medical schools and others have made over the doubling period, what we are seeing is a large increase in demand for grants at the time when the supply for grants is sort of flattening.

So the real tension right now is, how do you sustain a vibrant research enterprise across the board and at the same time look at issues like this one, which is a very valid issue to look at? That is what the tension is and that is where the budgetary decisions came up.

Senator HARKIN. Thank you, Dr. Zerhouni.

Thank you, Mr. Chairman.

Senator SPECTER. Thank you very much, Senator Harkin.

Senator Shelby.

AUTOIMMUNE DISEASES

Senator SHELBY. Thank you, Mr. Chairman.

I want to, doctor, focus on the area of autoimmune, specifically lupus. It is estimated that 1.5 million Americans suffer from lupus. Ninety percent of those being diagnosed are women. This is a terribly painful disease, as you well know. It has been about 40 years, it is my understanding, since a new drug has been developed and approved for treatment of lupus. Is there any hope in sight for new treatment, because this is in the area, as I understand it, of autoimmune, in which you do a lot of research?

So how do we—first, what do you see down the road there?

Dr. ZERHOUNI. This is an excellent, excellent question, in a field of research, autoimmune disease, that affects 5 to 8 percent of Americans. It is not just lupus, Senator.

Senator SHELBY. It is all autoimmune, is it not?

Dr. ZERHOUNI. Right, it is all autoimmune. It is a whole category of diseases that we are now beginning to understand. Break-throughs over the past year indicate that we may have actually developed technologies where we could develop—we could detect years before the disease really starts the markers of the disease and maybe intervene earlier.

What I would like to do is ask my colleague Dr. Fauci, who is the Director of the National Institute of Allergy and Infectious Diseases, who has a lot of knowledge in autoimmune diseases, to perhaps address some of that.

Senator SHELBY. That would be good. Thank you, doctor.

Dr. FAUCI. Thank you, Dr. Zerhouni.

Senator Shelby, there are some very promising areas in the whole arena of autoimmune diseases. There is still a long way to go, but, very briefly, as Dr. Zerhouni mentioned in his opening statement, it falls within that area of predictive and ultimately preemptive and preventive, in the sense that we now are developing

rapidly, not only with lupus, much more sensitive diagnostic tests that can give you a feel for the ultimate evolution of an autoimmune disease.

One among many therapeutic modalities that I would just submit for your consideration that we are very excited about is the whole area of what is called immune tolerance. Immune tolerance means that you manipulate the immune system to get it to not respond to a particular antigen. In other words, you tolerize it to it.

This has been something that has been very exciting in animal studies. Now, with a network involving multiple institutes within the NIH, the immune tolerance network, we have been able to tolerize the body against rejecting transplanted organs. We found very rapidly that that can be applied to diseases of autoimmunity.

PREDNISONE

Senator SHELBY. Is that what Prednisone does?

Dr. FAUCI. Well, Prednisone is a drug that dampens globally the immune system. But we are talking about when we talk about tolerance, specifically training the body either not to reject an organ that is transplanted or not to respond to tissues that are self tissues. Patients should not respond to self antigens, but for reasons that relate to genetic, environmental, and other factors, they inappropriately react against their own tissues.

So now we try to tolerize them and dampen the immune response only specifically for the particular tissue that they are attacking, not general immunosuppression, because one of the real problems with treating any autoimmune disease, if you induce a global immunosuppression you have a lot of complications that relate to immunosuppressive therapy, much the way cancer patients have complications related to chemotherapy.

LUPUS

Senator SHELBY. What could you say to the 1.5 million or more lupus sufferers out there right now in the pipeline?

Dr. ZERHOUNI. Well, if I may, Dr. Fauci, I would like to show you the evolution of our investments in lupus research.

What I want to tell you is that there is really hope because, one, we have made advances in genomics that allow us to now identify some genetic factors in patients with lupus. Two, we really understand the immune response very specifically and we believe that the T-cells that respond in lupus may be a target for treatments. We also have research that suggests that perhaps a viral connection exists as well.

So over the past 2 years, 3 years, there has been a multiplication of new ideas thanks to the doubling and many people looking at it. What we intend to do is sustain it. We have ideas of how to in fact focus on autoimmune diseases across NIH and do the basic research across all institutes that will serve every one of these diseases.

So, Senator, it is a difficult disease. It is not an easy disease. If you have known anyone with lupus—

Senator SHELBY. My wife.

Dr. ZERHOUNI. I am sorry, Senator. I did not know about that. It is something that we really care about.

Senator SHELBY. Thank you very much.
Mr. Chairman, thank you.

PROGRAM FUNDING

Senator SPECTER. Thank you, Senator Shelby.

Obviously, we would like to have a lot more time to go into greater detail on many subjects. But what we would appreciate your doing is giving us a supplemental memorandum as to what the cuts will mean for your ongoing programs. I would like to share that with all of our colleagues in the House. Second, what it would take to adequately fund the issues you are working on and what you could accomplish with the figure you put on as being adequate.

Dr. Zerhouni, your statistics are very impressive and the showing of a trillion dollars in savings compared to a modest investment, that is the kind of things Congress needs to hear. That is the kind of things which impresses the Congress.

[The information follows:]

PROGRAM FUNDING

Within the context of a deficit-reduction budget, the President's Budget request had to weigh many competing priorities, and still proposed to hold spending for NIH at a straightlined level for fiscal year 2007. In fiscal year 2006, NIH reduced all noncompeting Research Project Grant (RPG) awards by -2.35 percent, and the average cost of competing RPGs was held at the fiscal year 2005 level. The fiscal year 2007 President's Budget Request provides no inflationary increases for non-competing continuation awards and holds the average cost of competing RPGs to the fiscal year 2006 level, which could lead to an erosion of the research buying power of NIH research projects. Within its available funds, however, NIH is supporting the highest priority research activities, including making strategic investments in bio-defense, the NIH Roadmap, a new program for new investigators, and the Clinical and Translational Sciences Award program.

If additional funds were available above these priorities, such as an increase for fiscal year 2007 above the Biomedical Research and Development Price Index inflator of 3.8 percent, NIH would be able restore the buying power of its research program, and fund additional projects, from basic, translational, and clinical research to therapeutic development and advanced technologies. All of these activities could serve to advance our understanding of the mechanisms underlying human health and disease and contribute to improving human health. Examples of projects that were not funded in the President's Budget Request, but could be undertaken are as follows:

Large-scale Genome Study for Serious Mental Disorders.—This study could speed development of new effective treatments for the 13 million Americans suffering from seriously debilitating mental disorders that prevent people from participating in daily life at home, work, or social settings for over 80 days per year and results in early death or suicide for 30,000 individuals each year.

Schizophrenia Treatment Research.—This proposed study could build on recent advances in schizophrenia treatment to determine whether an early intervention of aggressive pharmacotherapy, combined with focused rehabilitative efforts, can prevent long-term disability and suffering of schizophrenia, devastating mental illness affecting 2.4 million adult Americans.

Protocols for Treating Autism Spectrum Disorders Early.—These studies could bolster efforts to determine the most effective treatment regimens to improve outcomes for children and families struggling with the life-long disability and pain of autism spectrum disorders.

The Atherosclerosis Prevention Trial.—Although drugs to lower low-density lipoprotein (LDL) cholesterol levels are known to reduce the risk of major adverse cardiovascular events, it is not yet known whether additional benefits can be realized by lowering LDL cholesterol beyond current treatment guidelines. A multi-center, randomized clinical trial could determine whether aggressive lowering of low-density lipoprotein cholesterol beyond current treatment guidelines further reduces major adverse cardiovascular events.

Program to Reduce Cardiovascular Disease Risk in Young Adults by Preventing Weight Gain.—Studies could develop and evaluate promising intervention ap-

proaches for preventing weight gain in young adults, which is a major risk factor for cardiovascular disease (CVD) and associated CVD risk factors including elevated cholesterol, high blood pressure, and diabetes.

Systolic Blood Pressure Intervention Trial.—Although drug treatment to lower blood pressure, both systolic and diastolic, is known to reduce CVD mortality, it is not yet known whether additional benefits can be realized by lowering systolic pressures beyond current treatment guidelines. A multi-center trial could determine whether treating systolic blood pressure to a lower goal than currently recommended further reduces cardiovascular disease mortality and morbidity, particularly for those aged 50 years and older in whom systolic blood pressure is more strongly associated with CVD risk than diastolic blood pressure.

PREPAREDNESS FOR PANDEMIC INFLUENZA

Senator SPECTER. Dr. Fauci, if you would supplement what you have testified to on pandemic flu. There is enormous concern in this country today and we would like to know to what extent are we prepared. Being prepared is a tough subject to answer, but to what extent are we prepared. When you say that more funding would be of material assistance, I think there is something that we are prepared to fund.

Senator Harkin took the lead and put a figure of \$7 billion. We came close to \$6 billion, and contracts have been let for five big companies for a billion dollars. It is scary. It could be devastating. So let us know, and this subcommittee is prepared to take the lead again.

[The information follows:]

PREPAREDNESS FOR PANDEMIC INFLUENZA

The Department has made great strides to improve the Nation's preparedness for a pandemic influenza outbreak. For example, HHS has stockpiled roughly 8 million doses of vaccine against one H5N1 virus strain. Given, a two-dose vaccination schedule, this would allow vaccination of 4 million people. The Department also recently invested more than \$1 billion in the development of cell-based vaccine technology; shifting from the current egg-based technology is critical to quickly producing vast quantities of vaccine should a pandemic develop. Our goal is to build the capacity to vaccinate all 300 million Americans within 6 months of a pandemic outbreak. The Strategic National Stockpile now contains sufficient antivirals to treat nearly 7 million people, and with another 19 million courses on order, it should contain 26 million courses by the end of 2006. HHS is also enabling States and other entities to purchase up to 31 million antiviral treatment courses off of the Federal contract. Our goal is to have enough antivirals on hand for 25 percent of the population, or approximately 75 million individuals. In addition, we have purchased 150 million N95 respirators, surgical masks and other personal protective equipment. Planning summits have been held in all but two States, and almost every State has either a draft or final pandemic flu plan in place. As Secretary Leavitt has stated, "Preparation is a continuum. Every day we prepare brings us closer to being ready. We are better prepared than we were yesterday. And we must be better prepared tomorrow than we are today."

The National Institute of Allergy and Infectious Diseases (NIAID) is a major component of these preparation efforts. For example, NIAID has made progress in the development of an H5N1 influenza vaccine. NIAID-supported researchers at St. Jude Children's Research Hospital obtained a clinical isolate of a highly virulent H5N1 influenza virus in Vietnam in early 2004, and used a technique called reverse genetics to create a non-virulent vaccine reference strain from this isolate. NIAID then contracted with sanofi pasteur and Chiron Corporation (now Novartis) to manufacture pilot lots of the inactivated virus vaccine for use in clinical trials. The sanofi pasteur vaccine has been tested in healthy adults and is currently in clinical testing in healthy elderly people and children. The Chiron vaccine is currently in clinical testing in healthy adults.

Results from the trial of the sanofi pasteur vaccine in healthy adults provide both good and sobering news. The good news is that the vaccine is well-tolerated, and induces an immune response that augurs well for protecting people against the H5N1 virus. The sobering news is that larger doses of the H5N1 vaccine than typi-

cally used for yearly influenza vaccine are needed to elicit immune responses in the majority of people that would be predictive of protection. However, preliminary results from a Phase I clinical trial of an H9N2 influenza vaccine candidate made by Chiron suggest that addition of an adjuvant—a vaccine component that increases the immune response—may help to reduce the required dose. Clinical trials of H5N1 candidates using adjuvants and other strategies to improve immune responses at lower doses of vaccine are ongoing or imminent.

In addition, NIAID intramural researchers are working with colleagues from MedImmune, Inc. under a Cooperative Research and Development Agreement (CRADA) to produce and test multiple vaccine candidates for potential pandemic influenza strains, including H5N1 strains. The researchers have developed three live-attenuated H5N1 vaccine candidates, designed for nasal spray delivery, that have been shown to be protective in mice. The CRADA capitalizes on the long history of NIAID research and development of respiratory virus vaccines, including fundamental research that was key to the development of FluMist®, the licensed nasal spray influenza vaccine manufactured by MedImmune. The researchers have produced a clinical lot of a candidate H5N1 vaccine based on a strain isolated in Vietnam in 2004, and clinical trial of this vaccine is expected to begin later this year.

NIAID also supports a number of basic and applied research projects that could lead to significant advances in the development and production of vaccines against potential pandemic strains of avian influenza. This includes investigation of cell culture-based vaccine production as an alternative to chicken egg-based vaccine production—as noted above, an endeavor to which the Department of Health and Human Services recently committed \$1 billion that was awarded to several pharmaceutical companies. In addition, NIAID conducts and supports research into new vaccine platforms, including recombinant subunit vaccines, in which cultured cells are induced to make various influenza virus proteins that are then purified and used in a vaccine; gene-based vaccines, in which influenza genetic sequences are injected directly into a person to stimulate an immune response; and vector approaches that insert the genes of influenza virus into another non-virulent virus (the vector) and inject the vector vaccine as a carrier to present the influenza proteins to the vaccine recipient. For example, a gene-based influenza vaccine developed by researchers at the NIAID Vaccine Research Center is expected to enter Phase I clinical trials later in 2006.

In addition to efforts to develop vaccines against potential pandemic influenza strains, NIAID is supporting basic and applied research to develop improved antiviral drugs against influenza. These efforts include a screening program for new drugs, as well as targeted drug development and clinical trials. NIAID-supported researchers are conducting studies of varying doses and combinations of existing antiviral medications, developing and testing long-acting next-generation antivirals, and evaluating novel drug targets for potential prevention and treatment of influenza using in vitro and animal models.

Because a pandemic influenza virus could emerge anywhere in the world, NIAID helps to conduct global surveillance and molecular analysis of circulating influenza viruses. For example, NIAID funds a long-standing program to detect the emergence of influenza viruses with pandemic potential, in which researchers in Hong Kong and at St. Jude Children's Research Hospital collect and analyze influenza viruses from wild birds and other animals in Asia and North America and generate candidate vaccines against them.

NIAID is also supporting a collaborative effort to release full genomic sequence information for several thousand influenza viruses to the public domain. More than 1,000 influenza viruses have been sequenced. Readily available sequence data will allow researchers to further study how influenza viruses evolve, spread, and cause disease, which may ultimately lead to improved methods of treatment and prevention; identify specific characteristics of previous pandemic strains, which may help focus preparedness efforts; and identify genes that are highly conserved among various strains, and therefore act as possible targets for broadly protective therapeutics or vaccines.

Lastly, NIAID is collaborating with Oxford University, the Wellcome Trust and the World Health Organization to establish a small network of clinical sites in Southeast Asia to conduct clinical research on avian influenza and other emerging infectious diseases. A key purpose of the effort is to build an independent clinical research capacity in these countries. Five sites in Vietnam, four sites in Thailand and two in Jakarta will be established.

Senator SPECTER. I had thought it would be helpful if you stayed to hear the other testimony, but now that we have given you this

homework your time is too valuable. So we will stay and forge on alone.

Thank you very much for coming in. Thank you for what you are doing for America and the world.

Senator SHELBY. Mr. Chairman, can I just take 1 second?

Senator SPECTER. Certainly.

Senator SHELBY. I just want to commend you for bringing all these people together. This is a blue ribbon panel if I have ever seen one and I have seen a lot of panels in the Congress, as you have. We appreciate what NIH has done and we will be ashamed of ourselves if we do not properly fund you for the benefit of the American people.

Senator SPECTER. That is high praise coming from Senator Shelby because he usually deals with bankers.

Senator SPECTER. Senator Harkin.

MULTI-BUG APPROACH ON VACCINES

Senator HARKIN. Mr. Chairman, I want to thank the panel and all the people from NIH for coming down here today.

Dr. Fauci, in your supplement that the chairman spoke to you about, I wanted to delve a little bit into the multi-bug approach on vaccines that I understand you are working on, rather than just the one bug, one vaccine approach. So I would like to know a little bit more about that and where that stands.

Dr. Collins, in regards to—there is some interesting work going on in terms of the relating of genes and environment. I know you are doing some stuff on that and I would also like to be kind of brought up to speed on that, too, if you could submit that.

Thank you.

[The information follows:]

MULTI-BUG APPROACH ON VACCINES

The National Institute of Allergy and Infectious Diseases (NIAID) is supporting research and development of alternate approaches to dealing with the threat of emerging and re-emerging infectious diseases such as influenza.

For example, NIAID is pursuing the development of a "universal vaccine" that protects against multiple virus strains such as those resulting from antigenic drift associated with seasonal influenza and antigenic shift associated with pandemic influenza. As influenza viruses circulate, the genes that determine the structure of their surface proteins undergo small changes. Sometimes the change in the genes results in a slight change in the antigenic properties of the protein, a process commonly referred to as "antigenic drift". Antigenic drift is the basis for the changes in seasonal influenza observed during most years, and is the reason that we must update influenza vaccines annually. Influenza viruses also can change more dramatically. For example, viruses sometimes emerge that can jump species from natural reservoirs, such as wild ducks, to infect domestic poultry, farm animals, or humans. When an influenza virus jumps species from an animal, such as a chicken, to infect a human, the result is usually a "dead-end" infection that cannot readily spread further in the human population. However, mutations in the virus could develop that allow human-to-human transmission. Furthermore, if an avian influenza virus and another human influenza virus were to simultaneously co-infect a person or animal, the two viruses might swap genes, possibly resulting in a virus that is readily transmissible between humans, and against which the population would have no natural immunity. These types of significant changes in influenza viruses are referred to as "antigenic shift." When an "antigenic shift" occurs, a global influenza pandemic can result. Historically, pandemic influenza is a proven threat. In the 20th century, influenza pandemics occurred in 1918, 1957, and 1968.

The NIAID is supporting a number of research projects to develop a vaccine that induces a potent immune response to the common elements of the influenza virus

that undergo very few changes from season to season and from strain to strain. Although this is a difficult task, such a “universal” influenza vaccine would not only provide continued protection over multiple seasons, it might also offer protection against a newly emerged pandemic influenza virus and thus substantially reduce the susceptibility of the population to infection by any influenza virus—making the country far less vulnerable to influenza viruses emerging from avian and other animal sources.

One relatively stable element of the influenza virus is a protein called M2. The external portion of the M2 protein is very similar in influenza viruses from year to year and from strain to strain. A “universal” influenza vaccine targeting the M2 protein, or other conserved elements, could be protective against a range of influenza strains. NIAID-supported researchers have demonstrated that vaccines made with bioengineered versions of M2 can protect mice from lethal influenza virus. The scientists now are testing cross-reactivity between different species and strains of influenza, examining how long the immunity provided by these vaccines lasts, and evaluating whether the influenza viruses can evade these vaccines by developing mutations in their M2 proteins.

In addition, researchers at the NIAID Vaccine Research Center (VRC) are developing and testing gene-based influenza vaccines that will protect against multiple strains of influenza. As a first step, initial candidate vaccines, each containing the gene encoding the hemagglutinin (H) surface protein of an influenza virus isolated from a recent human outbreak of influenza (H1N1, H3N2 or H5N1), have already shown promise in animal studies. VRC researchers plan to develop additional gene-based vaccines for all common variants of hemagglutinin, as well as other influenza viral proteins, such as nucleoprotein and the M2 protein. In future, the VRC will incorporate both conserved and variable genes from multiple influenza strains into DNA and adenovirus vectors that can readily be produced by existing manufacturing processes.

A second approach, while not technically a vaccine, is an immune enhancer which specifically targets a component of the immune system and enhances one’s ability to respond to a broad range of microbial threats. Studies of the human innate immune system, which is comprised of “first responder” cells and other defenses that provide a first line of defense against a wide variety of pathogens, have been moving forward rapidly. These advances suggest it may be possible to develop a relatively small set of fast-acting, broad-spectrum countermeasures that can boost innate immune responses to many pathogens or toxins, including influenza. The capability to boost the innate immune system also could lead to the development of more powerful vaccine additives, called adjuvants, that can increase vaccine potency. The concept of immune enhancers has been demonstrated in early stage clinical studies, but requires further research and development to be applied to pandemic influenza vaccination.

GENES, ENVIRONMENT, AND HEALTH INITIATIVE

On February 8, 2006, HHS Secretary Leavitt announced that the President’s budget proposal for fiscal year 2007 included \$68 million for the Genes, Environment and Health Initiative (GEI), a research effort by the National Institutes of Health (NIH) to combine a type of genetic analysis and environmental technology development to understand the causes of common diseases such as asthma, arthritis, many types of cancer, diabetes, and Alzheimer’s disease. This represents a \$40 million increase above the \$28 million already planned for such efforts by the NIH for fiscal year 2007.

If approved by Congress, \$26 million of the requested \$40 million increase in funding would go to genetic analysis and \$14 million to the development of new tools to measure environmental exposures that affect health. The discoveries made through these efforts can potentially lead to profound advances in disease prevention and treatment. By seizing the historic opportunity provided by the Human Genome Project and the International HapMap Project, this initiative would speed the discovery of genetic risk factors for common diseases. But, as it has been said, genetics loads the gun; environment pulls the trigger. GEI will also provide markedly improved ways to measure and analyze the environmental contribution to disease, so that we can understand the complex interplay among genes and environment that is responsible for all human health and disease.

The NIH has recently formed a Coordinating Committee of representatives from 13 Institutes and Centers that would develop the content, priorities, and implementation of the initiative, should it be approved by the Congress. Similar to the management of NIH Roadmap initiatives, specific functions of the Coordinating Committee include: (a) identification of research priorities and opportunities relevant to

the program, (b) guidance and support of the development and implementation of specific research initiatives related to the program, (c) evaluation of proposals for specific activities to be conducted under the auspices of the program, and (d) facilitation of appropriate NIH-wide communication of program goals, initiatives, and findings. Two subcommittees have been formed, one to focus on the genetics component of GEI and the other to focus on its environmental component. These subcommittees will do the necessary planning for the proposed program during the current year and will be prepared to help administer the initiative, provided fiscal year 2007 funds are made available. Attached is a breakdown of the proposed budget for the initiative. Since the initiative is so early in its planning stages, the number of grants that would be awarded eventually is not known at this time.

Through initiatives such as GEI, we stand on the threshold of creating a future that would revolutionize the practice of medicine by allowing us to predict disease, identify environmental triggers, develop more precise therapies and, ultimately, prevent the development of disease in the first place.

Senator SPECTER. Thank you all very much.

We turn now to our next panel: Dr. Knapp, Dr. Auerbach, Dr. Chao, Dr. Comstock, Dr. Emerson, Ms. Eng, and Dr. Fox.

We have taken the unusual step of inviting 20 witnesses to this hearing to give us a bird's eye view or a thumbnail sketch, to mix metaphors, as to what is happening in specific lines of medical research. We have allocated as much time as we can, consistent with the schedule. It is not enough.

Dr. Knapp represents the entire group on medical research and there has been an allocation of 3 minutes for him and an allocation for every other witness, regrettably, of only a minute and a half. But that is the best we can do, and you have submitted written statements, all of which will be made a part of the record, and that will give us an opportunity to have some insights on your views and what is happening in your specific fields.

We are going to just indicate the group you are associated with, as opposed to going over your curriculum vitae's, which are all very, very impressive. Dr. Knapp, we start with you, representing the Ad Hoc Group for Medical Research.

STATEMENT OF RICHARD M. KNAPP, M.D., CHAIR, AD HOC GROUP FOR MEDICAL RESEARCH

Dr. KNAPP. Good morning. My name is Dick Knapp and I chair the Ad Hoc Group for Medical Research.

Mr. Chairman, all Americans owe you and Senator Harkin an enormous debt of gratitude for your unwavering commitment to medical research and your continued leadership in the support of the NIH, and we applaud your efforts to add funds to the 2007 budget to permit a \$2 billion increase in NIH funding.

The President's budget claims to freeze NIH at the 2006 level, but for almost all NIH institutes and centers this budget represents a cut, not a freeze. This budget proposal represents the fourth consecutive year that NIH funding has failed to keep pace with inflation. In inflation-adjusted dollars, as you pointed out, Mr. Chairman, this budget represents a loss of almost 11 percent of purchasing power since 2003.

Mr. Chairman, we are well on our way to undoubling the NIH budget that you and your colleagues fought so hard to achieve. As you heard from Dr. Zerhouni, NIH-funded research is driving the transformation of the practice of medicine. At a time of unparalleled scientific opportunities and unprecedented health challenges, NIH should be positioned to support more research, not less. Yet,

under this President's budget NIH would fund 10 percent fewer competing research project grants in 2007 than 4 years ago.

Because new investigators are essential to NIH's future, as Dr. Zerhouni pointed out, NIH-sponsored training should be supported as a top priority. However, due to fiscal constraints, the NIH has been unable to meet the stipend recommendations it made in 2001, and the President's budget proposes no stipend increases in 2007.

The flattening of the NIH budget also undermines the Nation's biomedical research infrastructure. Mr. Chairman, and you Senator Harkin have emphasized the need for increased support for the renovation and construction of extramural research facilities and the acquisition of state of the art laboratory instrumentation. Yet this budget again fails to request funds for the NIH extramural facilities program and the budget proposes to cut funding for shared instrumentation grants by nearly 8 percent below the level of 2005.

This morning's witnesses will describe how NIH research has safeguarded and improved the lives of all Americans while at the same time serving as a catalyst for new products and technologies, creating skilled jobs and contributing to the Nation's economic growth.

PREPARED STATEMENT

We share your concern that the continued flattening of the NIH budget threatens further progress in all of these areas. Thank you for the chance to be here.

[The statement follows:]

PREPARED STATEMENT OF RICHARD M. KNAPP

Mr. Chairman and members of the subcommittee, my name is Dick Knapp, and I chair the Ad Hoc Group for Medical Research Funding, a coalition of more than 300 patient and voluntary health groups, medical and scientific societies, academic and research organizations, and industry. The Ad Hoc Group is pleased to have the opportunity to provide an overview of the President's fiscal year 2007 budget for the National Institutes of Health (NIH).

Mr. Chairman, the members of the Ad Hoc Group, and indeed, all Americans, owe you and Senator Harkin an enormous debt of gratitude for your unwavering commitment to medical research and your continued leadership in support for the NIH. We share your belief that much of what has been accomplished in the past half century to help save lives and improve the health of all Americans can be attributed, directly or indirectly, to the NIH. And we applaud your efforts to add funds to the fiscal year 2007 budget resolution to permit a \$2 billion increase in the NIH budget. In January, the Ad Hoc Group joined four other major medical research advocacy groups in calling for the NIH budget to be increased by a minimum of \$1.4 billion (5 percent) in fiscal year 2007.

The President's budget for fiscal year 2007 proposes \$28.35 billion in budget authority through this subcommittee for the NIH, which is an increase of less than \$1 million over the current year's level. Much has been made of this proposal for flat funding. But for most areas of research, this budget represents a cut, not a freeze. Under the President's proposal, the fiscal year 2007 budgets for almost all NIH institutes and centers would be reduced below the fiscal year 2006 levels.

In addition, it is important to recognize that this year's budget is not a one-year aberration. The President's overall request is \$64.5 million less than what NIH received in fiscal year 2005, and the proposed budgets for most institutes and centers are between 1 and 1.5 percent lower than two years ago. If adopted, the President's budget would represent the fourth consecutive year that NIH funding has failed to keep pace with inflation as measured by the Biomedical Research and Development Price Index. In fact, in terms of inflation-adjusted dollars, the President's budget represents a loss of 11 percent of purchasing power since 2003, as shown in the attached graph. Mr. Chairman, we are well on our way to "undoubling" the NIH budget that you and your colleagues fought so hard to achieve.

It is the cumulative effect of this multi-year “flattening” of the NIH budget that is cause for concern. The flattening has had and would continue to have a severe impact across the pillars of NIH: basic research, translational and clinical research, research training, and the research infrastructure.

NIH-funded researchers have blazed new trails for medical research. Basic research forms the knowledge foundation needed to achieve continued scientific advancement. And as you have heard from Dr. Zerhouni, the discoveries resulting from the investment in NIH-funded research are driving the transformation of the practice of medicine through the development of novel and personalized therapies, cures, and prevention strategies.

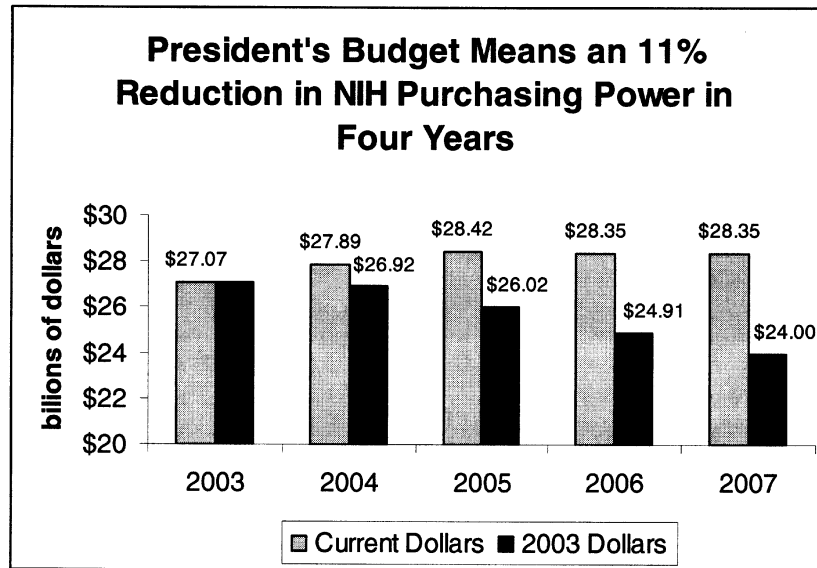
According to the Congressional Justification accompanying the President’s budget, in fiscal year 2007 NIH will be able to support 37,671 total research project grants (RPGs). This is 1,570 fewer RPGs than NIH funded in fiscal year 2004. What is more critical is the reduction in the number of new and competing RPGs. Under the President’s budget, NIH will be able to award 9,337 competing RPGs in fiscal year 2007, a decrease of 1,074 compared to fiscal year 2003. This is 10 percent reduction in just four years. At a time of unparalleled scientific opportunities and unprecedented health challenges, NIH should be positioned to support more research, not less.

In addition, a key function of NIH is to support training awards to encourage new investigators into basic and clinical medical research careers. Because an influx of new investigators is essential to NIH’s future, NIH-sponsored training opportunities should be supported as a top priority, with realistic funding levels for stipends, tuition, and benefits. Under the President’s budget, the NIH will be able to support 17,499 full-time training positions (FTTPs) in the Ruth L. Kirschstein National Research Service Award (NRSA) program. This is a reduction of 139 since fiscal year 2005. Furthermore, in 2001 the NIH recommended increased stipend support for NRSA recipients; however, the agency has been unable to meet these objectives due to fiscal constraints. For example, stipends for pre-doctoral students and post-doctoral fellows have fallen significantly short of NIH’s targets, and the President’s budget provides no increases for stipends above the fiscal year 2006 levels. How are we to continue to attract the best and brightest students with stipends that are unduly low in view of the high level of education and professional skills involved in biomedical research?

The flattening of the NIH budget also undermines the nation’s biomedical research infrastructure. NIH extramural research infrastructure grants are essential if research institutions are to update or replace aging research laboratories. Senator Harkin recognized the critical importance of the research infrastructure to the continued leadership of the United States in medical research when he championed the Twenty-First Century Research Laboratories Act, which was enacted in 2000. This legislation emphasized the need for increased support for the renovation and construction of extramural research facilities and the acquisition of state-of-the-art laboratory instrumentation. Yet once again, the President’s budget fails to request funds for the peer-reviewed, competitively awarded, extramural research facilities grant program administered through NIH’s National Center for Research Resources.

Federal funding also is critical to equip core facilities at biomedical research institutions with state-of-the-art technologies. NIH administers two competitive grant programs that award funds to institutions to purchase present and emerging technologies: the Shared Instrumentation Grant Program for groups of NIH-supported investigators to obtain commercially-available equipment that costs more than \$100,000; and the High-End Instrumentation Grant Program to acquire more expensive equipment, such as structural and functional imaging systems, electron microscopes, and supercomputers. These grants maximize the utility of federal research funds by allowing a number of scientists with similar instrumentation needs to share such equipment, and promote interactions among scientists, frequently across scientific disciplines, thereby catalyzing mutually rewarding new research collaborations. Yet, the President’s budget proposes to reduce funding for these programs to \$64.4 million, which is 7.7 percent below the fiscal year 2005 level.

This morning’s witnesses will give specific examples of how the research supported and conducted by NIH has had a profound and far-reaching impact on society in many important ways, serving as a catalyst for new products and technologies, creating skilled jobs, contributing to the nation’s economic growth, and most importantly, safeguarding and improving the lives of all our citizens. Mr. Chairman, we share your concern that the continued flattening of the NIH budget as proposed by the President threatens further progress in all of these areas.



Senator SPECTER. Thank you, Dr. Knapp.

Dr. Judith Auerbach, representing the Foundation for AIDS Research.

STATEMENT OF JUDITH AUERBACH, Ph.D., VICE PRESIDENT, PUBLIC POLICY AND PROGRAM DEVELOPMENT, AMFAR, THE FOUNDATION FOR AIDS RESEARCH

Dr. AUERBACH. Good morning, Mr. Chairman, and thank you very much. I am Judy Auerbach from amFAR and I will speak very quickly since we have only 90 seconds.

There are now more than 1 million HIV-infected people in the United States and the rates of HIV infection have risen dramatically among vulnerable populations, including racial and ethnic minority women and men. To make headway in the fight against AIDS, we need a strong Federal commitment to research leading to more effective treatment and prevention methods.

During the doubling of NIH's budget, the Agency was able to expand the knowledge base in basic research focusing on human immunology, macromolecular biology, structural biology, and behavioral research. This led to a dramatic increase in the number of vaccine and therapeutic candidates in the pipeline and to the implementation of crucial HIV prevention trials in populations most at risk of infection.

But much of this progress is in jeopardy with current and proposed cuts. Factoring in the recent recalculation, AIDS research at NIH was cut by about 2.4 percent between 2005 and 2006 and will be cut another 6 percent under the President's 2007 request. This has grave consequences for grants overall, for expanded trials of promising prevention technologies and therapeutics, and for new and seasoned investigators.

The number of R01's in AIDS research decreased by 5 percent in both numbers and dollars from 2005 to 2006 and would decrease even further in 2007. Under current budget constraints, it is anticipated that the AIDS clinical trials networks will be allocated only about 54 percent of what it is estimated they will need over the next 7 years. This means important effectiveness trials of new prevention technologies and new therapeutics will not be launched. Research institutes are losing potential new investigators and more experienced ones are demoralized, knowing that the majority of submissions are triaged and unscored and that funding is not likely until resubmission, even if then.

So altogether this means that important AIDS research will not be undertaken and people at risk for or living with HIV and AIDS will not have access to lifesaving interventions.

My time is over, so I will stop there. Thank you.

Senator SPECTER. Thank you, Dr. Auerbach.

Dr. Moses Chao, Christopher Reeve Foundation.

STATEMENT OF MOSES CHAO, M.D., CHRISTOPHER REEVE FOUNDATION

Dr. CHAO. Thank you, Mr. Chairman.

In the past 10 years we have witnessed a remarkable turnaround in neuroscience research. It used to be dogma that the adult spinal cord could not regenerate or recover from serious injury. But now through basic research we know of specific genes, proteins, and cells that can stimulate the repair of the spinal cord, and we are now ready to convert these findings into new therapies.

But the United States is falling behind because of the decrease in NIH funding. The decrease has affected many scientists, including my own lab, because the level of funding has actually dropped to 10 percent. What that means is 1 out of 10 grants is being funded and that has produced some drastic consequences, because many innovative applications and promising experiments are not supported or carried out.

More distressingly, there is a huge negative impact on the recruitment of our next generation of young scientists because of this discouraging situation. So we believe that this is the time to invest in basic research to advance the progress that we have made in this area. Christopher Reeve often argued that what we learn about spinal cord regeneration has direct implications to many diseases, including glaucoma, Alzheimer's disease, and Parkinson's disease. Therefore, to put the brakes on funding basic research will interfere with new scientific discoveries that will be aimed at improving the health of all Americans.

Thank you.

Senator SPECTER. Thank you, Dr. Chao.

Ms. Amy Comstock, Parkinson's Action Network.

STATEMENT OF AMY L. COMSTOCK, CHIEF EXECUTIVE OFFICER, PARKINSON'S ACTION NETWORK

Ms. COMSTOCK. Good morning. Thank you, Chairman Specter and Senators Harkin and Shelby. I am Amy Comstock, the Chief Executive Officer of the Parkinson's Action Network, and I am here on behalf of Parkinson's patients, their families, and all of the national Parkinson's organizations.

Parkinson's disease is now listed among the 15 leading causes of death in this country. Yet there is still no cure and no known treatments that even slow the progression of the disease. In fact, since the introduction of dopaminergic treatments nearly 50 years ago, our community is still struggling with mere variations of that treatment for this progressive disease.

Even with the introduction of deep brain stimulation for Parkinson's disease, we are still only responding to the symptoms of the disease and not doing that very well sometimes, and certainly not for a long duration.

So I am here this morning, quite frankly, to use the word that we are terrified of flat funding at NIH. Not only will flat funding eat into all forms of research currently under way at NIH, but we are particularly fearful that it will have a disproportionate impact on clinical and translational research, which is exactly the kind of research that we need the most.

Clinical research is very expensive to conduct, but it is what we have to have in order for treatments to make it through the drug development pipeline and become available to patients. For example, there is a handful of drugs slated for clinical trials right now at NIH that in fact may be what we need so badly. They may be compounds that can slow the progression of the disease.

PREPARED STATEMENT

We have to have these trials, but we cannot have them without funding. With flat funding, even if those trials are conducted—we have to do the math—other research would be cut at NIH. Therefore, we strongly support a minimum of 5 percent increase for NIH.

Thank you.

[The statement follows:]

PREPARED STATEMENT OF AMY L. COMSTOCK

Thank you Chairman Specter, Ranking Member Harkin, and distinguished members of the Subcommittee for convening this hearing on NIH appropriations. I am the Chief Executive Officer of the Parkinson's Action Network (PAN). PAN represents the Parkinson's community, including the more than one million Americans currently fighting Parkinson's disease (PD), and their families, and the national Parkinson's organizations, such as The Michael J. Fox Foundation for Parkinson's Research, Parkinson's Disease Foundation, National Parkinson Foundation, Parkinson Alliance, and American Parkinson Disease Association.

As I am sure you all know, PAN was instrumental in helping garner Congressional support for this Subcommittee's doubling of the NIH budget over five years during the late 1990's and early in this decade. We continue to work in conjunction with so many to prevent the proposed freeze in funding for NIH. Flat-funding would, in effect, constitute a significant cut, as the Biomedical Research and Development Price Index (BRDPI) is estimated to have increased by 5.5 percent for fiscal year 2005, and will likely increase by 4.1 percent for fiscal year 2006, and 3.8 percent in fiscal year 2007. Accordingly, in order to not lose ground in ongoing research, we support the medical research advocacy community's recommendation for a 5 percent increase above the fiscal year 2006 funding level for the National Institutes of Health.

We cannot turn our backs on our most promising research, which may happen if this funding is not provided. The Parkinson's community is particularly concerned with several clinical trials that may be eliminated without sufficient funding and direction.

These clinical trials are a part of a study going on at NIH right now that embody the kind of translational research most promising to the Parkinson's community and is desperately needed. NET-PD (Neuroprotection Exploratory Trials in Parkinson's Disease) is a trial to study compounds that may slow the progression of Parkinson's

disease. Research into treatments that might slow progression is particularly important as current treatments for PD alleviate some symptoms but do not slow progression of the disease. Despite the potential value, this program may be halted or cut back if NIH does not receive adequate funding. Yet, NET-PD is exactly the kind of translational research that we strongly support NIH aggressively pursuing.

We believe that there is hope for today's Parkinson's disease patients and their families. There are emerging therapies that should be pursued—even therapies that could potentially reverse the progression of the disease. These are the neuro-restorative therapies, such as neural growth factors, gene therapies, and tissue transplants including stem cells, which ultimately may restore function in patients suffering from Parkinson's disease as well as other neurodegenerative disorders. However, if this important research is not aggressively pursued it may take many more years than necessary to determine if this hopeful research may become much-needed therapies for today and tomorrow's Parkinson's patients.

On behalf of the Parkinson's community, I thank you for your continued interest in Parkinson's disease issues and your support for better treatments and a cure for Parkinson's. I would be happy to answer any questions you may have.

Senator SPECTER. Thank you, Ms. Comstock.

We turn now to Dr. Steven Emerson on the cancer issue. Give my regards and thanks to Dr. John Glick, my oncologist.

STATEMENT OF STEPHEN EMERSON, M.D., ASSOCIATE DIRECTOR FOR CLINICAL RESEARCH, ABRAMSON CANCER CENTER, UNIVERSITY OF PENNSYLVANIA HOSPITAL

Dr. EMERSON. Good morning, Chairman Specter, Senators Harkin and Shelby. My name is Steve Emerson. I am the associate director for clinical research at the Abramson Cancer Center at Penn. Our outgoing director, Dr. Glick, sends his regards. He is no stranger to this committee.

First off, I want to thank you all for your continued support for the health and welfare of this country by means of health care research over the past several years. Without your support, we could not have done what we have done. In the area of cancer where I work, I have seen in the 25 years I have been working a change where 25 years ago a cancer diagnosis was uniformly and relatively quickly fatal, to now where over half the patients who walk in my office know that they will live at least 5 years, if not be cured of their cancer.

But still we are only partway there and at this point cancer is still the largest cause of death in all Americans under the age of 85. It is still a huge killer. We have a long way to go.

Now, you have heard a lot about the issues with the doubling of the budget and yet where we are with the flat budgets going forward. I want to concentrate on just one part of that. One of my roles at Penn is head of training and the mentoring of the next generation of investigators. What you see with the budget being flat is actually a reduction in all new R01's being funded to this year the eleventh percentile, next year much lower. This is one-third the level of funding in terms of numbers of grants and chances of getting funded that it was even 3 years ago, and that is going to get worse next year.

Worse than that, the money per grant is being cut 30 percent off even the best grants. So the funds going in for new research have plummeted. That is the source of the panic you are talking about. So for new investigators that we have all invested in, the outlook for them for careers, for taking care of all of us and for finding new cures, it is hard to convince them what the future is. If we do not correct this, all of the goodwill and investment we have made in

the infrastructure with the road map, all the collaborative work, all the genomics and cancer that we have put this investment into will go to waste because we will not have a next generation of scientists to take advantage of it.

PREPARED STATEMENT

So thank you all again in the past and in the future for your efforts on preserving the NIH budget and its mission. Thanks again. [The statement follows:]

PREPARED STATEMENT OF DR. STEPHEN EMERSON

Good Morning, Chairman Specter, Senator Harkin, and Members of the Subcommittee. I am Stephen Emerson, Associate Director for Clinical Research at the University of Pennsylvania's Abramson Cancer Center, one of NIH's original comprehensive cancer centers funded by the National Cancer Institute three decades ago. Our outgoing Director, Dr. John Glick, no stranger to this Subcommittee, extends his regards and regrets his schedule did not permit him to appear this morning.

Thank you for the opportunity to speak with you today about efforts by scientists and clinicians in the ongoing fight against cancer, a disease that is the leading cause of death for Americans 85 years of age and younger. In the United States last year, 1 of every 4 deaths was from cancer. This illness claimed the lives of about 563,700 Americans, with approximately 1.4 million new cancer cases diagnosed.

These staggering figures should not, however, diminish the hope that exists for all those who fall victim to this disease from the dramatic progress we have made in this fight. When the Abramson Center opened its doors three decades ago, a cancer diagnosis was a near certain, imminent death sentence. But through the efforts of millions of people, and as a direct result of the steadfast support of this Subcommittee in robust funding for cancer research over the years, today about 60 percent of cancer patients can expect to live more than five years after diagnosis. Working with our colleagues in partnership with organizations like the American Cancer Society and the Friends of Cancer Research, there is an aggressive, day-to-day battle to reverse the devastating effect that cancer has on the lives of so many individuals and families—through research, prevention efforts and treatment.

That effort, however, is under assault, and at great risk, if the President's fiscal year 2007 budget for the National Institutes of Health, and its proposed allocation for the National Cancer Institute, is not reversed. In the Bush 2007 budget proposal, the NCI is slated to receive \$4.75 billion—a cut of nearly \$40 million, or almost 1 percent, below NCI's fiscal year 2006 level. That is a reduction of \$70 million cut from the fiscal year 2005 level and approximately \$186 million less than what the Congressional Budget Office estimates is necessary to maintain current projects, infrastructure and spending adjusted for inflation and other factors.

Within the proposed levels for the NCI, virtually every major activity, other than activities for the NIH Roadmap initiative, would be reduced. Cancer research activities would be cut \$50 million below the 2006 level, which itself was slightly reduced from the level allocated for 2005. Cancer biology research would be cut nearly \$41 million and research into the causes of cancer would be reduced more than \$6 million. Overall support for the cancer centers would be reduced by more than \$2 million, capping a two-year period of real decline in the NIH investment for its cancer centers. Even cancer control and prevention, one of the single most important areas in our efforts to combat this disease, is scheduled to be hit with a nearly \$2.5 million reduction, reductions that amount to a cumulative decline of nearly \$17 million over two years.

These proposed reductions, which I know you oppose Mr. Chairman, completely contradict the Administration's stated goal of ending suffering and death from cancer by 2015. They fly in the face of the spiraling cost of cancer treatment, pegged at more than \$72 billion annually in the United States, nearly five percent of all health care expenditures. And they send the wrong message to the nation at a time when the economic burden, excluding the costs for treatment, from cancer morbidity and premature mortality is a staggering \$120 billion annually.

For the community of scientists and clinicians who have dedicated their lives to the prevention, diagnosis and treatment of cancer, and who are the members of the team working in every state in our nation to meet that 2015 goal, these proposed cuts are both alarming and highly discouraging. If enacted, these funding levels would drop success rates for scientists proposing research project grants to the NCI

to just 16 percent—that is a 1 in 6 chance of obtaining funding. Such a level would mean a drop in the NCI grant success rate of more than 50 percent since 1998, and a drop of 43 percent since 2002. For NCI's R01 grants, the bread and butter mechanism for most NIH funded scientists, the payline for last year is even worse—just 11 percent. Reductions in 2007 would only erode that level further.

While older, more established research scientists will likely find a way to hold on to most of their core funds, the effect on young investigators—the seed corn of our future in this battle—is nothing short of devastating. The NIH New Investigators Committee presented data last December that showed the average age of a typical new NIH R01 awardee with an M.D. degree had reached 44. At the same time, the percentage of new investigators in competing R01 Awards across NIH continues to decline to just 20 percent. For the NCI, the first-time investigator success rate for all grant mechanism is worse—just 11 percent. For R01's, the success rate is again just 17 percent. The message these proposed cuts send is that for promising young biomedical professionals, a career focused on tackling cancer—whether in the fundamental study of genomics, proteomics, and biomarkers, or the more applied disciplines directed at generating new diagnostic or treatment regimes and devices—is not worth pursuing. The President's budget runs the risk of beginning the effective elimination of a whole generation of cancer scientists—at the very time when we are turning the corner on the fight against this disease.

Those of us who have spent our lives focused on ending the scourge of this disease know that this Subcommittee—more so than any other in the U.S. Congress—led the fight for funds to double the NIH budget. And there has been tremendous progress against cancer as the number of people who died from cancer between 2002 and 2003 decreased for the first time, the year corresponding to the last of the large NIH budget increases. The Director of the NCI, in his testimony to this Committee last month, outlined a number of significant scientific breakthroughs in the treatment and diagnosis of breast, ovarian and cervical cancers in just the last year. These continue the remarkable success we have had in fighting the number two cause of death in the United States.

The proposed 2007 budget cuts would help to unravel the progress this Subcommittee fought so hard to achieve in the doubling of NIH from 1998–2003. We urge you to redouble your efforts to stop them, and provide a modest increase—perhaps an additional \$300 million for the NCI in the coming year—to help offset declines enacted in 2006 and provide for most increases to sustain the pool of young scientists whose careers will hopefully be marked by the end of cancer as a scourge on so much of our nation and our world.

Thank you for the chance to present my views to the Subcommittee. We would be happy to prepare responses to any questions you might have for the record.

Senator SPECTER. Thank you, Dr. Emerson.

Ms. Lauren A. Eng, Spinal Muscular Atrophy Foundation.

STATEMENT OF LAUREN A. ENG, PRESIDENT, SPINAL MUSCULAR ATROPHY FOUNDATION

Ms. ENG. My daughter is one of the 33,000 American children suffering from spinal muscular atrophy, the most common genetic killer of young children. One missing gene causes nerves and muscles to wither away and most children die by the age of 2. But there are many terrible diseases. What makes SMA remarkable is the imminence of treatment. SMA represents both the problem and the opportunity of drug development for orphan diseases. Half of Americans with illness suffer from rare diseases and for the vast majority of rare diseases, especially pediatric ones, money and scientific advances are wasted because discoveries do not move from the bench to the bedside.

Because of scientific breakthroughs, NINDS chose SMA from its 600 diseases for a groundbreaking drug discovery program. The SMA project is a shining example that NIH can develop treatments and invest in further and basic science that is ripe and pays off. With less than \$5 million a year, a group of potential drugs have already been identified. NIH has been a catalyst of advancing re-

search and drug companies are interested. It achieved in 3 years what might have otherwise taken 10.

PREPARED STATEMENT

But running an astonishing race is useless if you stop short of the finish line. Under the proposed budget, continuation of the program is at risk. There is funding to pursue one drug, but scientists believe at least three should be advanced, each costing \$15 million to bring to trials. If NIH cannot fund this next step, it will have catastrophic effect. Academic and industry research will stop. We will have wasted the enormous investments and progress made in biomedical research, and for my child all of this is the difference between life and death.

[The statement follows:]

PREPARED STATEMENT OF LOREN A. ENG

I am Loren Eng, president of the Spinal Muscular Atrophy (SMA) Foundation and am here on behalf of the SMA Coalition. Most importantly, I am the mother of Arya Singh, who is one of the 30,000 children in America dying from Spinal Muscular Atrophy.

As you may know, SMA is a terrible disease. It is the most common genetic killer of babies and young children in America, and it is untreatable and fatal. It is often described as a genetic version of polio, or the children's equivalent of ALS. In children with SMA, one missing gene, and one missing protein causes motor neurons to die. Muscles weaken and wither away, leaving the bright minds of its young victims trapped by their failing bodies. Most children with SMA die within the first few years of life. Some are "lucky" and live longer, but face extreme disability and suffering.

But there are many terrible diseases. What makes SMA remarkable is the ability to truly make a difference with a modest amount of money and smart strategy.

SMA is a poster child for both the problem and the opportunity of drug development for rare pediatric diseases.

For large diseases, the historical focus on basic science works well—large drug companies take that basic science and translate it into treatments that save lives.

However, half of Americans with illness have smaller diseases, and for them the system has not worked. Breakthroughs are often achieved in basic science, but there are no large drug companies waiting to turn those breakthroughs into treatments. For a handful of smaller diseases, drug companies will only get involved at later stages where perceived risk is lower. But for most small diseases, the basic science is wasted because of the challenges of advancing research from the bench to the bedside. This is especially true for rare pediatric diseases. Money is spent, but children still die.

In the past decade, scientists studying SMA have achieved incredible breakthroughs, creating a unique opportunity to develop treatments. To its credit, NINDS has recognized the opportunity and taken steps to advance basic science with a revolutionary translational research effort.

Just three years ago, the NINDS designated SMA, from among 600 diseases, as the best candidate for a model new program to translate basic science into actual drugs and treatments. The SMA Project combined academic and industry expertise, and was a focused and strategic effort to translate remarkable science into real solutions.

In just three years, and for less than \$5 million per year, the SMA Project has brought us within reach of an effective treatment. Investigators have identified a group of potential drugs that may slow the progression of the disease. Despite a miniscule budget for the project, NINDS has made incredible strides in harnessing the community's efforts toward a near term treatment.

Unfortunately, running a brilliant race is useless if you stop before the finish line, and that is what we fear is at risk of happening.

I am not an expert in the federal budget but I do know that:

- this model SMA program would never have been initiated under this budget,
- the existing funding of just \$5 million a year is at risk, and
- the very success of the program is at risk.

The next phase of the project is pre-IND studies but there is only enough funding to study JUST one compound. Project scientists say we need at least two to three, and each costs \$2 million. For clinical trials we will need \$10 to \$15 million each.

The leadership of the NIH has been a catalyst of incredible progress—it expects to advance research to a point when they can be “handed off” to drug companies to fully develop. For a fraction of the vast amounts spent on caring for SMA victims, we could develop treatments that would save them. With a modest amount of money and continued focus, we can save lives, and money.

If NIH can not provide for these critical next steps, it will have a domino effect elsewhere:

- Young investigators will not focus on SMA,
- Existing non-government research will stall,
- Industry will surely not engage, and
- Other diseases like ALS and DMD will not reap the benefits of SMA research.

The SMA Project has been a revolutionary effort and a shining example of how NIH cannot only fund basic research but actually DEVELOP TREATMENTS for deadly diseases.

Through a solution driven approach, the NIH has achieved in 3 years what might have taken a decade. “Smart investment” could pay off in treatments that save lives. This is an incredible example of finding solutions, not just spending money. Of course, in this case, a “solution” means treatment that could save the lives and reduce the suffering of 30,000 children.

We urge you not to stop short now when we are so close. Reducing funding for NIH, and for projects like the SMA Project will have devastating consequences—we will waste the enormous amounts of money that have been spent and progress that has been made. For our daughter, it could mean the difference between life and death.

Senator SPECTER. Thank you, Ms. Eng.

We turn now to Dr. Philip Fox, American Association for Dental Research.

STATEMENT OF DR. PHILIP C. FOX, DIRECTOR OF CLINICAL RESEARCH, DEPARTMENT OF ORAL MEDICINE, CAROLINAS MEDICAL CENTER ON BEHALF OF THE AMERICAN ASSOCIATION FOR DENTAL RESEARCH

Dr. Fox. Thank you, Mr. Chairman. I am Dr. Phil Fox and I am really representing the dental research community.

I would like to highlight this morning some advances in salivary diagnostics, an area you have not heard much about. Diagnosis of most health conditions requires a blood or a urine sample and that may be invasive or painful to obtain. But now, after many years of research, saliva is poised to be used as a noninvasive diagnostic fluid for a number of oral and systemic conditions.

Dental researchers have been able to amplify molecular signals that are present in saliva, heralding the advent of new tests that allow for earlier diagnosis than is currently possible. Saliva is already being used routinely for rapid noninvasive HIV diagnosis and saliva-based tests will soon be available to detect oral cancer. Further, saliva has the potential to detect exposure to chemical and biological weapons and is being looked at in autoimmune diseases as well.

Now, most of this research is funded by the National Institute of Dental and Craniofacial Research, the NIDCR. However, as you have heard, the investment that is made in the NIH doubling is now at risk. I think that we have the research equivalent now of being all dressed up and nowhere to go.

As a result of your past investment, there are many unprecedented opportunities in dental research. But the austere budget of the last 4 years has resulted in a steady decrease in new research grants and many young investigators who are leaving the field.

Imagine a future in which a saliva sample is used for quick, painless and less expensive diagnostic tests and to monitor many systemic health conditions and exposure to chemical and biological weapons. Early diagnosis could save thousands of lives. We need you to sustain your commitment to NIH and to dental research in order to realize these unprecedented scientific opportunities.

Thank you for your interest and support.

Senator SPECTER. Thank you very much, Dr. Fox.

Unless there is some question from the panel, we will turn now to our next group of experts.

Thank you all very, very much.

Dr. KNAPP. Thank you.

Dr. EMERSON. Thank you.

Senator SPECTER. We now call on Ms. Patricia Furlong, Dr. Sam Gandy, Ms. Ann Gibbons, Dr. Robert Goldstein, Dr. Lawrence Holzman, and Dr. Steven Houser.

Thank you all very much for joining us. As is the situation with all of the witnesses, your full statements will be made a part of the record. We turn first to Ms. Patricia Furlong, who represents the Project on Muscular Dystrophy. Ms. Furlong.

STATEMENT OF PATRICIA FURLONG, CO-FOUNDER AND CHIEF EXECUTIVE OFFICER, PARENT PROJECT MUSCULAR DYSTROPHY

Ms. FURLONG. Thank you very much, Senator Specter, Senator Harkin, and Senator Shelby. I so appreciate this opportunity to talk about NIH funding.

I thought I would start by giving you three examples. In 1999 a scientist from the University of Pennsylvania with NIH support looked at aminoglycosides to suppress premature stop codons. Premature stop codons in a genetic sentence could be interpreted as a period in the middle of a genetic sentence, creating the loss of a significant protein. These aminoglycosides are found to suppress a premature stop.

This particular scientist went to industry and, again with his own NIH support, began high throughput screens. Today we have a drug in trial called PTC-124. This drug has implications for all genetic diseases in terms of a subset of the population with premature stops. It is currently in trial and demonstrating pharmacological activity in cystic fibrosis and in Duchenne muscular dystrophy we do not have the data. But this drug has sweeping potential results across the rare genetic disease community.

In 2000 a scientist from Johns Hopkins University looked at muscle regulators and found that inhibiting myostatin would improve the bulk of the muscle and potentially the strength. This drug is currently in trial in muscular dystrophies FSH, Becker, and myotonic.

In the year 2001, the Bowman-Burke inhibitor compound was looked at. It is a protease inhibitor that can slow or halt muscle degeneration in muscular dystrophy. It had been in trial in the National Cancer Institute and was halted, not because of any risk to the patient, but primarily due to lack of material. This drug is now going into trial through NIH funding in muscular dystrophy in January.

PREPARED STATEMENT

It is these cures, potential treatments for all of us, that make such a difference in our lives. We ask you to commit to NIH funding to supply that NIH, that research enterprise, with the funding it needs to help all of us, to give us time with the people we love, and to help not only the American people but people across the world.

Thank you.

[The statement follows:]

PREPARED STATEMENT OF PAT FURLONG

Good morning/afternoon Mr. Chairman and Members of the Committee, and thank you for this opportunity to testify on the NIH budget.

My name is Pat Furlong, Co-Founder and CEO of Parent Project Muscular Dystrophy and the mother of two sons who battled Duchenne Muscular Dystrophy.

Thanks to the significant amount of basic research funded by NIH in recent years, we are making encouraging progress in our quest to develop effective treatments for this always-fatal disease. Right now, we are in a Phase II clinical trial on a promising drug for a subset of patients with Duchenne muscular dystrophy, and potentially a subset of patients with many other genetic conditions.

It's basic NIH-funded research that served as a foundation and provided the spark for this drug, and many other promising therapies that are in the works. Without adequate NIH funding to support basic research, the medical research tower will rise much lower before eventually buckling due to the tremendous strain placed on too few resources.

We are particularly concerned about the negative impact the budget crunch will have on young investigators seeking to enter the field of Duchenne MD research. The budget limitations we have seen over the past few years have made it tremendously more difficult for young, first-time investigators with meritorious submissions to secure an R01 grant.

I urge your panel and the entire Senate to continue to lead the way in restoring critically needed dollars to support basic NIH research.

Senator SPECTER. Thank you very much, Ms. Furlong.

We now turn to Dr. Sam Gandy, representing the Alzheimer's Association.

STATEMENT OF SAM GANDY, M.D., Ph.D., CHAIR, MEDICAL AND SCIENTIFIC ADVISORY COUNCIL, ALZHEIMER'S ASSOCIATION

Dr. GANDY. Mr. Chairman, members of the subcommittee: As a direct result of this subcommittee's leadership and foresight, scientists supported by the NIH have made enormous strides towards understanding Alzheimer's, a disease that affects 4.5 million Americans today and will affect as many as 16 million in a few decades.

For the first time in the history of medicine, we have Alzheimer's genes in hand and we can now contemplate rational therapy for Alzheimer's. With adequate resources, scientists will be able to develop medications that modify Alzheimer's pathology in as few as 3 years. Achieving that goal will relieve a major bottleneck and attract every major pharmaceutical company to begin bringing new drugs into human clinical trials.

The current trajectory of NIH cuts threatens to arrest progress and devastate the upcoming generation of scientists. Current grants are now routinely cut by 18 percent. In my institution this is already causing layoffs and I see my students turning away from research careers. Budget cuts also mean that some of the most promising drug targets will go unstudied. An important new molecule was discovered just last month. Where will we find the resources to study its potential therapeutic value?

PREPARED STATEMENT

The inescapable conclusion is that Federal budget cuts are killing more than programs. These cuts are killing the minds of millions of Americans. The threat of Alzheimer's is staggering in its scope. I urge you and your colleagues to act now to reverse the disastrous path upon which we find ourselves.

Thank you very much for providing me with this opportunity to testify.

[The statement follows:]

PREPARED STATEMENT OF SAM GANDY

Mr. Chairman and members of the Subcommittee, I appreciate the opportunity to be here to discuss Alzheimer's disease, a disease that, as we speak today, is robbing 4.5 million Americans of their abilities to form memories and thoughts. The disease will ultimately take the life of every one of these 4.5 million. Within a few decades, as many as 16 million Americans will have Alzheimer's, all of whom will eventually succumb to the disease, unless we all, together, take up the fight toward a cure or means of prevention.

As a direct result of the leadership and foresight of this Subcommittee, the National Institutes of Health have played essential roles in developing and maintaining a cadre of American scientists such as myself who have made enormous strides toward understanding Alzheimer's and, for the first time in the history of medicine, contemplating rational interventions aimed at the underlying disease process. We now know that Alzheimer's is a disease and not an inevitable consequence of aging. We have identified several key genetic mistakes that are so malignant that one single mistake in the DNA is sufficient to cause the complete picture of Alzheimer's. These DNA mistakes have been both necessary and sufficient to supply us with essential information that has eluded scientists for the century since Alois Alzheimer presented his landmark paper in Munich in 1906. For the first time in the history of medicine, we are now able to mimic the earliest steps in the disease using chemicals, cells, or, most valuably, the lowly laboratory mouse. Human Alzheimer genes have enabled us not only to create in the laboratory a living brain with Alzheimer's, but, astoundingly, we are also now able to cure experimental Alzheimer's in the laboratory. These experimental therapies are now entering human trials so that we might translate these experimental cures into practical medicines for humans.

To date, four drugs have been approved for treating the symptoms of Alzheimer's, but these drugs only help a few patients, and even then, only modestly and temporarily. Current Alzheimer drugs leave the basic underlying disease untouched and the natural progression from amnesia to death proceeds along the standard, predictable, inevitable, and cruel path that we know all too well. Yet, from the laboratory, for the first time, scientists and physicians see genuine, tangible, quantifiable hope. Most experts agree that with adequate resources, scientists will be able to develop medications that will modify Alzheimer's pathology within the next three years. If the prevailing wisdom about the root cause of the disease is validated, a major bottleneck will be relieved, and every major pharmaceutical company will begin bringing new drugs into human clinical trials.

But that can only happen if you and your colleagues sustain the Alzheimer research enterprise. Alzheimer's drug development will certainly be stymied if Congress adopts the President's proposal, where for the fourth consecutive year the NIH budget fails to even keep pace with inflation.

The NIH doubling process is directly responsible for the progress of Alzheimer's research as a field of study: the field has moved from a backwater of obscurity into perhaps the single most visible, most competitive, and most exciting research field in experimental neurology. Within three years after this Subcommittee first appropriated funds for Alzheimer's, the number of scientists drawn into this field of study increased three-fold. But because of budget cuts over the past three years we are already seeing talented scientists turning to other fields.

The current trajectory of cuts threatens to devastate the upcoming generation of scientists. NIH funding of the scientists who populate the faculties of our universities is not simply used to buy test tubes and chemicals: those funds directly pay the salaries of scientists on these faculties. Draconian cuts will render these scientists and professors unemployable. And with the loss of this talent, we are postponing the day that we can eradicate this deadly disease.

But perhaps most importantly, persistent budget cuts are shutting out opportunities to find ways to cure or prevent Alzheimer's disease. In 1998, NIH was funding 30 percent of top-rated grant applications. Today, the percentage of Alzheimer projects that actually receive funding is down to 18 percent. Some institutes are struggling to maintain 10 percent funding. This means that most scientific opportunities are being left on the table. It also means that some of the most promising clinical trials—the tools we need to translate basic research findings into effective clinical treatments—will be delayed or scrapped altogether. The inescapable conclusion, for me, at least, is that federal budget cuts are killing more than programs; they are killing the minds of millions of Americans.

Mr. Chairman and Senator Harkin, I am certain that you both realize that we cannot be a strong nation unless we are a healthy nation. In fiscal year 2007, spending on all Medicare beneficiaries benefits will total \$449.2 billion. Unless we find a way to prevent or cure Alzheimer's disease, in less than 25 years, the care of Medicare beneficiaries that is attributed to Alzheimer's alone will cost over \$400 billion, roughly equivalent to today's entire Medicare budget. The threat is so enormous that the temptation is to just give in to nihilism and cynicism. I urge you and your colleagues to join us in resisting this temptation and act now to reverse the disastrous path upon which we find ourselves.

Thank you for the opportunity to testify.

Senator SPECTER. Thank you. Thank you, Dr. Gandy.

Our next witness is Ms. Ann Gibbons, representing Autism Speaks.

STATEMENT OF ANN GIBBONS, MEMBER, BOARD OF DIRECTORS, AUTISM SPEAKS

Ms. GIBBONS. I am the mother of a 17-year-old boy with autism and I am a member of the board of directors of Autism Speaks, and I am here to speak for those who cannot.

Autism is our Nation's fastest growing developmental disorder, affecting 1 in 166 children, up more than tenfold from a decade ago and costing our Nation approximately \$35 billion annually. Autism has no known cause, no known cure, and few effective treatments. The incidence of autism has increased at epidemic proportions, but NIH funding for autism research has been frozen over the past 2 years and will remain so in the President's 2007 budget.

Specifically, the first lost opportunity is developing new treatment standards for autism. This would support research on new or existing early interventions to establish common methods of verifiably effective treatment. Early intervention provides children with the best possible opportunity to develop in the most normal way possible, but not with the President's budget, where this critical research will not be funded.

Another lost opportunity is defining the core features of autism, when it begins, its long-term course, and subtypes of the disorder that may exist on the autism spectrum. Understanding the common features of autism will lead to identification of its causes, both genetic and environmental, and identify better treatments or even prevention of the disease. The President's proposed budget will not fund this research.

PREPARED STATEMENT

The incidence of autism will continue to grow, but funding for autism research will not. With the President's budget, opportunities will be lost, but the pain and suffering of autistic children and their families will continue to grow, as will the cost to society.

I just want to thank you all for what you are doing for biomedical research.

[The statement follows:]

PREPARED STATEMENT OF ANN GIBBONS

Mr. Chairman, I am Ann Gibbons, a resident of Bethesda, Maryland, a member of the Board of Autism Speaks, and the mother of a 17-year-old son with autism.

Autism Speaks was launched to help find a cure for autism by raising the funds to facilitate and quicken the pace of research, to raise public awareness of autism, and to give hope to all those who suffer from this disorder. Autism Speaks' goal is to give a voice to an entire community, to every family dealing with the hardships of autism. With its mergers with the National Alliance for Autism Research and the Autism Coalition for Research and Education, Autism Speaks now represents our nation's largest autism advocacy organization.

In both of my roles, in my public capacity as an Autism Speaks board member and in my private role as a mother of an autistic child, I commend you, Mr. Chairman, for your leadership in promoting funding for biomedical research and support you in your efforts to secure increased funding for the National Institutes of Health this year.

Funding for understanding the causes of and finding treatments for autism is sorely needed. Autism is our nation's fastest-growing developmental disorder, now affecting 1 in 166 children in the United States, up more than tenfold from just a decade ago. A Harvard School of Public Health professor, in a recent book, estimates that it can cost \$3.2 million to care for an autistic person over the course of his or her lifetime, and by conservative estimates autism costs our society \$35 billion annually in direct and indirect costs.

Autism has no known cause, no known cure, and few effective treatments. And while NIH funding for autism may have tripled in the past decade to \$100 million, that amount pales in comparison to the money spent for research on other diseases and disorders that affect fewer individuals.

Autism research is poised at a turning point. While diagnoses are skyrocketing at epidemic rates, many areas of autism research stand on the verge of important findings. If adequately funded, this research could yield real progress on the diagnosis, treatment and cure for this disorder. The President's proposed freeze on NIH funding falls short on all counts, and would seriously impede the progress and promise of autism research.

One turning point is the development of new treatment standards for autism spectrum disorder. This program would support research on new or existing interventions with the goals of establishing common methods of treatment and measurements of treatment efficacy. This study could hasten the ability to use existing treatments early to improve outcomes for children and families struggling with the disability of autism spectrum disorders. When autistic children do receive evidence-based early intervention service between ages 3 and 5, from 20 to 50 percent of them are able to go onto mainstream kindergarten. Early intervention is critical in order to provide children with autism the optimum opportunity to develop in the most normal way possible.

Unfortunately, Mr. Chairman, the President's proposed budget for fiscal year 2007 will freeze funding for autism, and research leading to advances in autism intervention will not be possible.

Another turning point is the need to define core features of autism, including when it begins, its long-term course, and subtypes of the disorder that may exist on what is known as the autism spectrum.

Defining the features of autism could lead toward the long-term goal of finding genetic and non-genetic causes of autism and offering the possibility of providing better treatments or even prevention of the disease. It's also urgent that we better understand the genetic associations with autism so that research into the interaction of genes with the environment can be understood.

With the budget proposed by President, this research will not be funded, and these advances cannot be made.

With the President's budget, progress in understanding brain development and autism, one of the most devastating disorders affecting hundreds of thousands of children, will be slowed or halted. Scientists will be unable to realize the full potential of the latest scientific techniques, in neuroimaging and genetics technology.

Mr. Chairman, autism, which the Centers for Disease Control and Prevention estimates now affects 300,000 American children between ages 4 and 17, will continue to grow, with 3 children now being diagnosed every hour. The pain and suffering of autistic children and their families will continue, as will the costs to society. But research on this devastating disorder will be stymied, progress on potential treat-

ments and cures will be stymied as a result of the President proposed freeze on spending for biomedical research and on research on autism.

Moreover, we will lose the opportunity to save an entire generation of children from this devastating disorder, which can lock people in their own worlds, unable to communicate with, and sometimes unable to experience the affection of those who love them.

Mr. Chairman, thank you for giving me the opportunity to speak for those with autism and their families.

Senator SPECTER. Thank you. Thank you very much, Ms. Gibbons.

Our next witness is Dr. Robert Goldstein, representing the Juvenile Diabetes Research Foundation.

STATEMENT OF ROBERT GOLDSTEIN, M.D., Ph.D., CHIEF SCIENTIFIC OFFICER, JUVENILE DIABETES RESEARCH FOUNDATION

Dr. GOLDSTEIN. Thank you, Senators Specter, Harkin, and Shelby for this opportunity to testify. I am Robert Goldstein, the chief scientific officer for the Juvenile Diabetes Research Foundation.

Without an increase in Federal funding for diabetes research, there will be a disproportionate impact on clinical translation research. Islet cell transplantation, a procedure that has been successfully done experimentally in nearly 600 diabetes patients, will delay the—the NIH-sponsored clinical trials to expand this proven treatment out into the community will be seriously delayed.

In the area of hypoglycemia, dangerously low blood sugar can lead to convulsions, coma, or even death. The Diabetes Research and Children's Network's efforts to assess new glucose monitoring technology will impact on the management of type 1 diabetes in children.

Diabetic retinopathy. Anti-angiogenesis drugs that can reverse diabetic retinopathy have been discovered, but clinical trials to extend and expand these findings to test new classes of drugs would be delayed or halted.

Treatment of new onset of type 1 diabetes. Clinical trials using monoclonal antibodies have shown that insulin-secreting cells can be protected for up to 2 years. Support studies to determine how to prolong this effect, whether treatment prior to the onset can prevent diabetes, and whether these therapies can be given years after onset would be delayed or curtailed. Since type 1 diabetes is an autoimmune disease, this will impact understanding of other autoimmune diseases.

PREPARED STATEMENT

Causes of type 1 diabetes. NIH-supported efforts to identify the genes responsible for susceptibility will be curtailed and delay our ability to effectively prevent disease in at-risk populations.

Thank you for the opportunity to testify.

[The statement follows:]

PREPARED STATEMENT OF ROBERT GOLDSTEIN

Chairman Specter, Ranking Member Harkin and Members of the Subcommittee, thank you for the opportunity to testify before you today regarding the many opportunities that will be lost without an increase in federal funding for diabetes research at the National Institutes of Health. I am Robert Goldstein, the Chief Scientific Officer for the Juvenile Diabetes Research Foundation International.

In the past 25 years, the number of people with diabetes has more than doubled, so that today approximately 20.8 million Americans have diabetes. Evidence sug-

gests that 1 in 3 Americans born in 2000 will develop diabetes during his or her lifetime. Diabetes is the 6th leading cause of death in the United States. The disease cost this country \$132 billion in 2002, which is almost 5 times NIH's annual budget. Only research to better prevent, treat and cure diabetes will significantly impact these numbers.

The Diabetes Research Working Group recommended \$1.6 billion in fiscal year 2004—the last year of their study—to take advantage of the many diabetes research opportunities. We have used appropriations to build critical momentum for accelerating the delivery of therapies to people with diabetes. There have been major advances (see attached) and more importantly programs have been put in place that will insure continued advances. Yet funding today is \$600 million short of this recommendation. Absent an increase in federal funding, this momentum will be lost and progress and solutions will be delayed. Specifically, the following areas of diabetes research will be seriously impacted:

Islet Cell Transplantation.—Nearly 600 diabetes patients worldwide have now received islet transplants, and enough patients have been transplanted that long-term benefits can be documented. Islet cell transplants have resulted in significant benefits to people with very complicated forms of type 1 diabetes: for instance, at least half of the transplant recipients exhibit stabilization or reversal of their diabetic eye and nerve diseases. Overall, islet transplant patients report a significant improvement in their quality of life. However, challenges remain, and we need additional funding for NIH programs and NIH/CMS sponsored clinical trials to test new protocols and fully understand how to maximize this proven treatment so it is an appropriate therapy for all who suffer from type 1 diabetes.

Hypoglycemia.—Hypoglycemia—episodes of dangerously low blood sugar—is the most feared acute complication of diabetes and can lead to shaking, convulsions, coma, or even death in extreme cases. Young diabetic children who may not be able to recognize or communicate the signs of impending hypoglycemia are especially vulnerable. Technologies coming onto the market in the near term have the ability to warn patients of hypoglycemia, and it is critical that the technology is suitable for use in children. The NIH has established the Diabetes Research in Children Network (DirecNet) to provide independent assessments of glucose monitoring technology and its impact on the management of type 1 diabetes in children, and this important work would be delayed without additional funds.

Diabetic Retinopathy.—Diabetes is the leading cause of new blindness in working age adults; more than 8.5 million people in the United States have diabetic retinopathy or eye disease. Significant progress being made on the causes and pathogenesis of diabetic retinopathy is generating renewed hope for the prevention or reversal of eye disease. For the very first time anti-angiogenesis drugs that can actually reverse diabetic retinopathy, as opposed to simply halting further progression by means of laser treatment, have been discovered. The NIH-supported Diabetes Retinopathy Clinical Research Network (DRCR.Net) includes more than 150 collaborating physicians across the United States, and provides an organized platform for rapidly translating new therapeutic ideas from the research community into clinical testing in human patients. Clinical trials to test the pipeline of potential new drugs would be delayed, curtailed or halted without continued funding.

Treatment of New Onset Type 1 diabetes.—By the time type 1 diabetes is diagnosed, patients have already suffered a devastating autoimmune attack that has destroyed most of the insulin-producing beta cells of the pancreas. Research has shown that a patient's level of residual beta cell activity correlates with the ability to more easily maintain glucose levels close to normal and reduces the amount of insulin that must be injected. A prime research goal is to develop new therapies that will help newly diagnosed type 1 diabetes patients preserve remaining beta cells and possibly even dampen the immune system enough to allow the pancreas to regenerate new beta cells. Researchers have identified a drug that can effectively alter the clinical course of the disease. A short 1–2 week course of treatment with an antibody—named anti-CD3—helps patients maintain or increase their ability to produce insulin naturally for up to 18 months after diagnosis compared to a placebo. This treatment demonstrates the proof of principle that the clinical source of an established autoimmune disease can be significantly altered. This work could not have been done without the major advances in clinical trial platforms from several NIH sponsored programs, including:

—Immune Tolerance Network, whose goals are to develop new therapies to treat/prevent autoimmune disease and to prevent or treat graft rejection in transplantation by inducing immune tolerance. Among the diseases under investigation by this collaborative effort include type 1 diabetes and islet transplantation; and

—TRIAL NET which also supports studies aimed at both preventing further destruction of insulin secreting cells in new onset type 1 diabetes, as well as developing the means to prevent disease.

More extensive studies to determine how long this effect can be maintained, and whether the addition of specific antigen therapy or other drugs can prolong this effect, will not occur without continued support. Similarly, large studies to determine whether early treatment prior to disease onset can prevent diabetes or whether these therapies can be given years after disease should be supported.

Genetics and Environmental Causes of Type 1 Diabetes.—The best way to attack type 1 diabetes is to stop it before it ever starts, but this requires sophisticated knowledge of the underlying causes of disease. Ground breaking NIH efforts (T1DGC, TEDDY, TRIGR) to identify the genes responsible for susceptibility to type 1 diabetes coupled with the identification of environmental triggers (viruses, toxins, dietary factors) will be curtailed or abandoned without continued funding, and delay our ability to effectively prevent disease in at-risk populations.

Diabetes research has demonstrated a strong return on the federal investment. Continued strong federal commitment is needed.

Thank you again for the opportunity to appear before you today. I am happy to answer any questions you may have.

THE NIH AND DIABETES RESEARCH—A STRONG RETURN ON FEDERAL INVESTMENT

Diabetes affects more than 20 million adults and children in the United States, up to 7 percent of the population. In 2001, approximately \$3.8 billion was spent on inpatient care for diabetes; two-thirds of those costs could have been saved with appropriate primary care for complications. A 2002 study estimated that diabetes—both type 1 and type 2—caused the U.S. economy \$132 billion in direct medical costs and indirect costs such as disability, work loss, and premature mortality. The disease accounts for more than 30 percent of Medicare expenditures. Total diabetes costs are predicted to climb to as much as \$192 billion per year by 2020.

Beyond the economic impact is the personal toll that diabetes exacts. Individuals with diabetes have twice the prevalence of disability as persons without diabetes. In 2002, more than 176,000 cases of permanent disability were attributed to diabetes at an estimated cost of \$7.5 billion. That same year diabetes accounted for 88 million disability days. Persons with diabetes are at greater risk for stroke, heart attack, blindness, kidney failure, limb amputation, nerve damage, severe dental disease, and complications of pregnancy. Type 1 diabetes can reduce a person's expected lifespan by as much as 15 years.

The Diabetes Control and Complications Trial (DCCT), a clinical trial of 1,441 people with type 1 diabetes, demonstrated that tight control of blood glucose through intensive insulin therapy could significantly reduce or delay many diabetic complications. This landmark finding spurred a shift in the daily management of type 1 diabetes and energized research in the field. In 1996, at the conclusion of the DCCT, it was estimated that implementation of intensive insulin management in the entire U.S. diabetic population would save 920,000 years of sight, 691,000 years free from end stage kidney disease, 678,000 years free from amputation, and 611,000 years of life.

Since the discovery of insulin more than 80 years ago, biomedical research has continued to improve the health and lives of diabetes patients. The research listed below demonstrates that the field of juvenile diabetes research is making advances worthy of a continued strong federal investment.

—*Advances in Islet Cell Transplantation.*—Since 1999, almost 600 diabetes patients worldwide have received islet transplants, and enough patients have been transplanted that long-term benefits are beginning to emerge. This procedure involves isolating the insulin-producing cells, called islet cells, from a donor pancreas, and injecting them into an adult who has juvenile diabetes. Islet cell transplants have resulted in significant benefits to people with very complicated forms of type 1 diabetes: for example, at least half of patients exhibit stabilization or reversal of their diabetic eye and nerve diseases. Overall, islet transplant patients report a significant improvement in their quality of life. Unfortunately this procedure cannot be used in children because the medications that need to be taken to prevent the body from rejecting these donated cells can have many side effects. Researchers are working to improve this procedure and to develop new techniques so that one day the procedure can be suitable for children with juvenile diabetes.

—*Treatment in new Onset Type 1 Diabetes.*—Researchers have identified a drug, a monoclonal antibody, that can effectively alter the clinical course of type 1 diabetes: a short 1–2 week course of treatment with the antibody—named anti-

CD3—helps patients maintain or increase their ability to produce insulin naturally for up to 18 months after diagnosis compared to a placebo. Treated patients required reduced insulin dosage, and better hemoglobin A1c levels. A larger phase II trial of this procedure is underway. These findings are significant because residual beta cell activity correlates with the ability to more easily maintain glucose levels close to normal, and to prevent the development of the devastating complications of diabetes. Anti-CD3 is at the leading edge of a robust pipeline of potential therapies for reversing new onset type 1 diabetes. The Type 1 Diabetes TrialNet was established in 2001 to “fast track” potential diabetes therapies into clinical trials.

- Advances in Preventing Hypoglycemia.*—Significant advances in glucose monitoring technology help patients to determine whether their blood sugars are falling (signaling the need to eat to avoid hypoglycemia) or rising (indicating the need for an insulin dose). Researchers have evidence that patients who use continuous glucose monitoring systems spend more time in the normal glucose range; a critical finding because short term variability in glucose levels may be as important as overall, long-term glucose control in predicting the risk of complications. In 2005, an NIH-funded study validated that newer-generation home blood glucose meters demonstrated a high degree of accuracy over a broad range of glucose concentrations in children with type 1 diabetes. The study was conducted by Diabetes Research in Children Network (DirecNet), a network of clinical centers that provides an independent assessment of glucose monitoring technology and its impact on the management of type 1 diabetes in children. DirecNet is now testing the new continuous glucose monitors, which will be the next wave in diabetes care and represent an essential step toward an artificial pancreas.
- Reversing of Diabetic Retinopathy.*—Diabetes is the leading cause of new blindness in working age adults. Laser treatment can reduce the risk of severe vision loss by 20 to 50 percent and saves up to \$1.6 billion per year by preventing or treating diabetic eye disease. New research has discovered anti-angiogenesis drugs that can actually reverse diabetic retinopathy, as opposed to simply halting further progression by means of laser treatment. These and other new classes of drugs make up a pipeline that must be tested in clinical trials.
- Preventing Cardiovascular Disease.*—Adults with diabetes are two to four times more likely to have a stroke or to die from heart disease than adults without diabetes. Indeed, heart disease or stroke is the leading cause of death among patients with diabetes, accounting for 65 percent of deaths in this population. Blood pressure control reduces the risk of heart attack and stroke by 33 to 50 percent and the risk of other complications by as much as 33 percent. Nevertheless, additional research is necessary to understand the factors that contribute to increased cardiovascular risk. New findings to design new diagnostic tools that predict or detect the early onset of cardiovascular disease, develop new drugs or devices to reverse cardiovascular damage due to diabetes, and clinically test new therapies in large, randomized trials.
- Slowing Onset and Progression of Kidney Disease.*—Diabetes is the leading cause of kidney failure in the United States, accounting for 44 percent of new cases in 2002. Based on NIH-funded research, scientists have made great progress in developing methods that slow the onset and progression of kidney disease in people with diabetes. Drugs used to lower blood pressure (antihypertensive drugs) can slow the progression of kidney disease significantly. Two types of drugs, angiotensin-converting enzyme (ACE) inhibitors and angiotensin receptor blockers (ARBs), have proven effective in slowing the progression of kidney disease. Drugs that lower blood pressure, including ACE inhibitors or angiotensin receptor blockers (ARBs), decrease the onset of kidney disease by 30 to 70 percent.
- Gaining an Understanding of Kidney Disease Susceptibility.*—Some diabetic patients seem to be particularly susceptible to developing diabetic nephropathy, while others show no signs of kidney damage even after many years of living with diabetes. Researchers are actively investigating the genetic factors that influence an individual’s susceptibility or resistance to diabetic nephropathy. The Genetics of Kidneys in Diabetes (GoKinD) Study has gathered more than 2,600 participants for the study of the genetic risk factors for type 1 diabetes and diabetic kidney disease. This sample and data collection will provide a resource to facilitate investigator-driven research into the genetic basis of diabetic kidney disease. Furthermore, GoKinD participants form the core of a population registry that could be recruited for future clinical trials.
- Reducing Incidence of Diabetic Neuropathy.*—Two-thirds of all diabetes patients suffer from some degree of nerve damage affecting organs throughout the body.

This condition—known as diabetic neuropathy—results in loss of sensation, weakness, or pain in hands or feet, carpal tunnel syndrome, pain in the eyes or face, pain in the chest or abdomen, profuse sweating, loss of balance or coordination, slowed digestion of food or related gastrointestinal problems, urinary incontinence, erectile dysfunction, and a variety of other nerve problems. The inability to feel pain coupled with impaired wound healing often leads to non-healing foot ulcers and, ultimately, amputation of some part of the foot or leg. For this reason, diabetic neuropathy is the most common cause of non-traumatic lower limb amputation. Comprehensive foot care programs to detect and treat skin ulcers before they progress can reduce the rate of amputation by 45 to 85 percent.

- Understanding Susceptibility to Disease.*—The Type 1 Diabetes Genetics Consortium (T1DGC) will identify the genes responsible for susceptibility to type 1 diabetes, leading to a better understanding of pathways to disease. Researchers recently confirmed the discovery of a new gene that contributes to susceptibility to disease. The pathway controlled by this gene implicates it in other autoimmune diseases, not just type 1 diabetes, underlining that common pathways may be involved in the development of autoimmunity. This understanding may lead to better diagnosis and new therapies to stop diabetes before it ever starts.
- Identifying Environmental Causes of Type 1.*—The Triggers and Environmental Determinants of Diabetes in Youth (TEDDY) study has screened more than 6,000 newborns to identify the environmental causes of type 1 diabetes in genetically susceptible individuals. Once completed, the TEDDY study will have amassed the largest data set and samples on newborns at risk autoimmunity and type 1 diabetes anywhere in the world.
- Investigating Vaccine to Prevent Type 1.*—Recent studies in animal models have raised the possibility that a “vaccine” may be able to prevent type 1 diabetes.
- Monitoring Progression of Type 1 Onset.*—Researchers have developed a means to non-invasively monitor the start and progression of insulinitis, the inflammation of insulin producing cells, in mice, which may allow researchers to predict whether and when individual people will develop type 1 diabetes in the future.
- Regenerating of Insulin Producing Cells.*—Replacement of the lost beta cells through either transplantation of islets from an external source or regeneration of islets within a patient's own pancreas is required to restore physiological control of glucose and cure type 1 diabetes. Development of regenerative treatments to restore beta cells without transplantation will require researchers to understand how beta cells are normally formed in the adult pancreas, and then use that information to identify molecular targets for drugs that can induce that process in diabetic patients. Researchers supported by the NIH Beta Cell Biology Consortium are now uncovering multiple pathways by which new beta cells are formed in the body. The work should help clarify how pancreatic beta cells develop, and it could potentially lead to successful treatments for both type 1 and type 2 diabetes.
- Identifying Animal Models for Complication Studies.*—The Animal Models of Diabetic Complications Consortium (AMDCC) has identified more than 70 animal models for the study of diabetic complications, including a number of promising models for type 1 diabetic cardiomyopathy, nephropathy and neuropathy.

Senator SPECTER. Thank you, Dr. Goldstein.

We now turn to Dr. Lawrence Holzman, representing the NephCure Foundation.

STATEMENT OF LAWRENCE B. HOLZMAN, M.D., CHAIRMAN, SCIENTIFIC ADVISORY BOARD, NEPHCURE FOUNDATION

Dr. HOLZMAN. Mr. Chairman and members of the subcommittee: Despite advances in dialysis and kidney transplantation, kidney failure remains a devastating diagnosis, carrying a survival prognosis similar to patients diagnosed with cancer and assuring a lifetime of severe medical complications.

NIH-sponsored investigators have been really remarkably successful in advancing our understanding of kidney disease, with the goal of preserving and preventing kidney functional loss. For example, a recent revolution in our knowledge of the biology of the kidney filter has allowed the identification of several inherited dis-

eases and promises to provide tools that will better allow us to diagnose and treat kidney failure in general.

However, cutting the NIH budget for kidney disease research or even failing to keep up with inflationary costs threatens present research momentum. As an investigator and as a member of an NIH peer review committee that evaluates scientific proposals, I can assure you that the effects of a restricted NIH budget are already being felt. Threatened by a pay line at which only 12 percent of grant applications are funded, investigators are reluctant to take risks necessary to dramatically advance the field. Delays in funding outstanding proposals retard progress and result in loss of uniquely trained research personnel.

PREPARED STATEMENT

Finally, despite NIH set-asides designed to protect junior investigators, our next generation of talented young people observe the anxiety created by funding uncertainty, make rational economic decisions, and turn away from a career in biomedical science.

Therefore, we ask you to provide an increase of 5 percent in fiscal year 2007 to the NIDDK and to the NIH budget overall.

Thank you for your attention.

[The statement follows:]

PREPARED STATEMENT OF LAWRENCE HOLZMAN

Mr. Chairman, and members of the Subcommittee, thank you for giving me this opportunity to come before you today. I am Dr. Lawrence Holzman, Associate Professor of Internal Medicine and Director of the NIH-sponsored Nephrology Training Program at the University of Michigan Medical School. I also serve as Chairman of the Scientific Advisory Board of the NephCure Foundation (NCF), a non-profit organization dedicated to fighting idiopathic nephrotic syndrome and focal segmental glomerulosclerosis (FSGS).

Fifteen million Americans have significantly impaired kidney function and are at risk of losing their kidney function entirely. Another 400,000 have already lost their kidney function. Despite NIH-sponsored advances in dialysis and kidney transplantation, kidney failure—due to common diseases such as diabetic kidney disease or hypertension, or due to relatively rare diseases such as focal segmental glomerulosclerosis—remains a devastating diagnosis. Kidney failure carries a shortened survival similar to that of many cancers and assures a lifetime of severe medical complications. The American people spend nearly \$20 billion per year to provide medical care for these individuals alone. Undeniably, there remains a critical need to prevent patients from losing kidney function.

Recognizing this need, NIH-sponsored investigators have made great strides in the basic science and clinical science of kidney disease, progress that has begun to slow the incidence of kidney failure. For example, during the past decade, a revolution in our understanding of the biology of the kidney filter sparked by initial successes in molecular genetics has allowed the identification of several inherited diseases of the kidney filter and promises to provide tools that will much better guide diagnosis and treatment of the patients who are likely to lose their kidneys. Dramatic advances in our understanding of the biology of cystic diseases of the kidney such as polycystic kidney disease has led to promising clinical trials of medications that might slow or prevent these diseases. For those patients that have already lost their native kidneys to disease, NIH-sponsored research has improved our understanding of the immune system, providing hope for kidney transplant patients who suffer the dangerous side effects of present day anti-rejection medications and who suffer from the knowledge that the average kidney transplant lasts only 11 years. Moreover, dialysis patients have improved quality of life because NIH sponsored clinical research has taught nephrologists how to better care for their patients.

Cutting the NIH-budget for kidney disease research, or even failing to keep up with the inflation in costs for doing this research, immediately threatens the research momentum that was attained by doubling the NIH budget. As an independent investigator, and as member of an NIH peer review committee that evalu-

ates independent-investigator initiated scientific proposals, I can assure you that the affects of a restricted NIH budget are already being felt in a real but difficult to quantify fashion. Threatened by a “pay line” at which only 12–14 percent of grant applications are funded (rather than 24 percent just three years ago), investigators have become reluctant to take risks that must be taken in their research that would dramatically advance a field. Delays in funding outstanding proposals (because they must be recycled through the application process several times before they are funded) retard progress and result in the loss of talented and uniquely trained research personnel that cannot be readily replaced. Finally, despite NIH set asides designed to protect junior investigators, our next generation of talented young people observe the anxiety created by funding uncertainty, make rationale economic decisions, and turn away from a career in biomedical science, leaving the future of this science in jeopardy.

NIH sponsored biomedical research is an American treasure that reaps multifold benefits; it is a treasure that must be nurtured and protected. Therefore, we ask you to provide an increase of 5 percent in fiscal year 2007 for the National Institute of Diabetes, Digestive, and Kidney Diseases (NIDDK), and the NIH overall.

Thank you.

Senator SPECTER. Thank you, Dr. Holzman.

Our final witness on the panel is Dr. Steven Houser, representing the American Heart Association.

STATEMENT OF STEVEN R. HOUSER, Ph.D., DIRECTOR, CARDIOVASCULAR RESEARCH CENTER, TEMPLE UNIVERSITY SCHOOL OF MEDICINE ON BEHALF OF THE AMERICAN HEART ASSOCIATION

Dr. HOUSER. Thank you, Senator Specter and Senators Harkin and Shelby. I am an American Heart Association volunteer for the last 30 years. My day job is at a cardiovascular research group at Temple University School of Medicine in North Philadelphia. My NIH-funded research focuses on how we can fix broken hearts so that people can live healthier, happier lives.

Thanks to your investments, I believe we are on the threshold of making wonderful discoveries that can be translated into novel therapies. My lab group works on a very simple concept. We have found that in every one of your hearts there are stem cells that are making new myocytes and blood vessels all the time. I believe that we have the opportunity to figure out ways to take these cells from each of your hearts, expand them, prime them to repair your heart, and save them in case you ever need them if your heart becomes damaged.

PREPARED STATEMENT

Unfortunately, the NIH cuts are limiting my ability and the ability of my collaborators in Pennsylvania, Iowa, which I just visited last week, and Alabama, where I will visit in about a month, to pursue these ideas. It is forcing me to cut my staff, train fewer people, lay off local workers. I think this has impact not just on science and medicine, but on the economies of the communities and the States that we are charged to serve.

So thank you so much for all your hard work with respect to these issues, and I would be happy to answer any questions.

[The statement follows:]

PREPARED STATEMENT OF STEVEN R. HOUSER

SUMMARY OF RECOMMENDATIONS

Agency	Amount
National Institutes of Health	\$29,800,000,000
National Institutes of Health Heart Research	2,200,000,000
National Institutes of Health Stroke Research	357,000,000
National Heart, Lung, and Blood Institute	3,100,000,000
National Institute of Neurological Disorders and Stroke	1,600,000,000
Agency for Healthcare Research and Quality	440,000,000
Centers for Disease Control and Prevention (plus funding for pandemic influenza preparedness)	8,500,000,000
Heart Disease and Stroke Prevention Program	55,000,000
Health Resources and Services Administration: Rural and Community Access to Emergency Devices Program	8,900,000
Department of Education: Carol M. White Physical Education Program	100,000,000

An estimated 71 million American adults suffer from heart disease, stroke, and other forms of cardiovascular disease. Nearly 2,500 Americans die of cardiovascular disease each day—an average of one death every 35 seconds. Heart disease and stroke remain the first and third leading causes of death, respectively, for both men and women in the United States today and more than half of men and nearly 40 percent of women will develop cardiovascular disease during their lifetime. As the baby boom generation ages, the prevalence of cardiovascular disease will increase dramatically, because although this disease can strike at any stage of life—the likelihood increases with age. Deaths from heart disease alone are projected to increase by about 130 percent between 2000 and 2050, according to one report.

Cardiovascular disease also costs Americans an estimated \$403 billion in medical expenses and lost productivity in 2006—more than any other disease and more than the projected budget deficit for that year. As the population ages, the combination of demographics and high costs will result in a cardiovascular disease crisis with staggering implications for health care costs and quality of care.

Although progress has been made in the treatment of cardiovascular disease, there is no cure. In fact, studies suggest that increased rates of diabetes, obesity and other risk factors may reverse four decades of declining mortality. The most prudent way to address this looming crisis is to simultaneously invest in prevention and in the development of more cost-effective treatments. Regrettably, the funding levels proposed by the President undermine efforts in both of these areas.

When adjusted for biomedical research inflation, the proposed NIH budget for cardiovascular disease research is estimated to be 15 percent lower in 2007 than in fiscal year 2003. Funding levels proposed in the budget for the CDC's Heart Disease and Stroke Prevention Program remain flat at a time when only 14 states receive the resources necessary to implement prevention programs and strategies. In addition, the Rural and Community Access to Emergency Devices Program, administered by the Health Resources and Services Administration, is terminated in the President's budget. This program provides grants to rural areas and communities to purchase and place AEDs in schools, churches, fire stations, and other locations to save the lives of cardiac arrest victims.

Now is the wrong time to reduce our nation's investment in programs that prevent and treat America's leading and most costly cause of death. Solving a problem of this magnitude will require a significant public investment in these fiscally challenging times, but if we fail to take aggressive and deliberate action now—we will pay a terrible cost later—both in terms of health care expenditures and human lives. The following recommendations from the American Heart Association address this problem in a comprehensive but fiscally responsible manner.

INCREASE FUNDING FOR THE NATIONAL INSTITUTES OF HEALTH (NIH)

NIH-sponsored research has revolutionized patient care and holds the key to an eventual cure for all forms of cardiovascular disease. Research funded by the NIH also fuels innovation that generates economic growth and preserves our nation's role as a world leader in the biomedical and biotechnology industries. For fiscal year 2006, NIH funding was cut below the previous year's level for the first time in 35 years. The President preserved this cut in his fiscal year 2007 budget and reduced NIH further over the next five years by nearly 20 percent. This five year cut reduces NIH resources in inflation adjusted terms by more than one-third from its peak in fiscal year 2003—the end of the historical five-year doubling of the NIH budget.

Recommendation.—The AHA joins the research and patient advocacy community in recommending an fiscal year 2007 appropriation of \$29.8 billion for the NIH. This level, which represents a 5 percent increase over 2006, covers the increased costs of biomedical research inflation and provides additional resources to investigate emerging research opportunities.

INCREASE FUNDING FOR NIH HEART AND STROKE RESEARCH

From 1993–2003, death rates from cardiovascular diseases have fallen by 22 percent, death rates from coronary heart disease have declined by 30 percent, and death rates from stroke have fallen by 19 percent. NIH sponsored heart and stroke research has improved health outcomes and in some cases, lowered health care costs. Examples of recent NIH-supported research follow.

Aspirin Prevents Another Type of Stroke.—Aspirin is as effective as, and safer than, the blood thinning drug warfarin in preventing intracranial arterial stenosis—which accounts for roughly 10 percent of all strokes. Aspirin is a low cost therapy that does not require the intricate and costly monitoring like the drug warfarin. Researchers estimate that use of aspirin rather than warfarin could cut health care costs by \$20 million each year.

Blood Test to Screen for Stroke Wins FDA Approval.—A blood test to screen for heart disease gained approval to predict stroke risk. The test scans the blood for levels of the enzyme lipoprotein-associated phospholipase A2, which are higher in potential stroke victims.

Diuretics Again Initial Therapy for High Blood Pressure.—Continuing analyses of the Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT) for diabetics, blacks and non-blacks with high blood pressure confirms, the initial conclusion that diuretics should be the initial high blood pressure treatment instead of newer, more costly drugs.

Antibiotics do not Prevent Second Cardiovascular Events.—Results of clinical trials have shown that antibiotics are ineffective in preventing second events like heart attack, unstable chest pain and stroke in patients with existing heart disease. This finding was unanticipated.

Slightly Elevated Blood Pressure Triples Heart Attack Risk.—Examining data from the Framingham Heart Study, researchers found that the 59 million Americans with prehypertension, blood pressures ranging from 120–139 over 80–89 mm Hg, are three times more likely to suffer a heart attack and nearly twice as likely to experience heart disease than those with normal blood pressure. Scientists estimate that aggressive treatment would prevent 47 percent of heart attacks.

Although cardiovascular disease is the leading cause of death in the United States, the NIH heart and stroke research budget remains disproportionately underfunded compared to the burden of these diseases on society. Cardiovascular disease meets NIH's priority setting criteria (public health needs, scientific quality of research, scientific progress potential, portfolio diversification and adequate infrastructure support), yet only 7 percent of the NIH budget is invested in heart research and a mere 1 percent is dedicated to stroke. Adjusted for medical research inflation, resources for cardiovascular research will decline 15 percent since fiscal year 2003 if the President's budget is enacted. These declining resources are insufficient to support and expand current activities and to invest in promising initiatives to aggressively advance the battle against heart disease and stroke. Additional funds would be used in the following areas:

Atherosclerosis Prevention Trial Network.—Atherosclerosis is a major risk factor for heart disease and stroke. With increased funding, the National Heart, Lung, and Blood Institute (NHLBI) could initiate a clinical trial to determine whether reducing low-density lipoprotein cholesterol, so-called "bad" cholesterol, to a level lower than currently recommended, reduces major cardiovascular disease events in healthy patients at high risk of heart disease and or stroke.

Systolic Blood Pressure Intervention Trial.—High blood pressure is a major risk factor for heart disease, heart failure and stroke. More funding would allow the NHLBI to conduct a multicenter clinical trial to determine whether reducing systolic blood pressure to a lower level than currently recommended could prevent heart attacks and strokes.

Preventing Weight Gain in Young Adults.—Young adults are at a high risk for weight gain. With more resources, NHLBI could develop and test innovative practical, cost-effective ways to prevent weight gain in young adults to prevent cardiovascular disease.

Stroke is the No. 3 killer of Americans and a major cause of permanent disability. In addition to the elderly, stroke also strikes newborns, children and young adults. An estimated 700,000 Americans will suffer a stroke this year, and nearly 158,000

will die. Many of America's 5.5 million stroke survivors face debilitating physical and mental impairment, emotional distress and huge medical costs; about 1 in 4 survivors are permanently disabled.

As a result of fiscal year 2001 Congressional report language, the National Institute of Neurological Disorders and Stroke (NINDS) convened a Stroke Progress Review Group. A report from this group provides a long-range stroke strategic plan for stroke research that includes 5 research priorities and 7 resource priorities. Multiple scientific programs initiated since the report have made impressive progress; however, additional funding is needed to implement the plan. The fiscal year 2007 estimate for NINDS stroke research falls 50 percent short of the target for implementation of that year of the plan. Additional funds would be used to conduct stroke research in the following areas:

Stroke Translational Research.—Translational studies are vital to providing cutting-edge stroke treatment and prevention. Due to budget shortfalls, the NINDS has been forced to compress its Specialized Programs of Translational Research in Acute Stroke (SPOTRIAS) from the planned 10 extramural centers to the five currently funded. SPOTRIAS researchers facilitate translation of basic research into patient care and evaluate and treat victims rapidly after the onset of stroke symptoms.

Neurological Emergencies Treatment Trials Network.—Limited resources will also force the NINDS to scale back its Neurological Emergencies Treatment Trials Network. This initiative is designed to develop a clinical research network of emergency medicine physicians, neurologists and neurosurgeons to develop more and improved treatments for acute neurological emergencies, such as stroke, through clinical trials.

Stroke Education.—As a member of the Brain Attack Coalition—a group of organizations devoted to fighting stroke—the AHA works with the NINDS to increase public awareness of stroke symptoms and the need to call 9–1–1. Together, we initiated a public education campaign, Know Stroke: Know the Signs, Act in Time, and we are striving to develop systems to make tPA available to appropriate patients. In partnership with the CDC, the NINDS extended this campaign to launch a grass-roots program called Know Stroke in the Community to enlist the aid of “Stroke Champions” who educate communities about stroke signs and symptoms. When these measures are implemented, stroke treatment will shift from supportive care to early brain-saving intervention. Additional funds are needed to educate the public and health providers about stroke.

Recommendation.—The AHA recommends an fiscal year 2007 appropriation of \$2.2 billion for NIH heart research. We advocate for an appropriation of \$3.068 billion for the NHLBI. And, we recommend \$357 million for NIH stroke research. We advocate for an appropriation of \$1.612 billion for the NINDS. These appropriations represent a 5 percent increase over fiscal year 2006—commensurate with the Association's overall recommended funding increase for the NIH.

INCREASE FUNDING AT THE CENTERS FOR DISEASE CONTROL (CDC)

Basic research must be translated into easy-to-understand guidance so that people can apply it to their daily lives. Prevention is the best way to protect Americans' health and ease the financial burden of disease. Although the clinical literature indicates that increased and improved cardiovascular disease interventions can be highly successful, investigators have concluded that well-established strategies for combating cardiovascular disease are often not being implemented. Recent studies suggest that not smoking, maintaining a healthy weight, and avoiding diabetes, high blood pressure and high cholesterol, may add 10 years to life.

The AHA commends Congress for supporting CDC's new Division for Heart Disease and Stroke Prevention, which provides funding to 33 states to create programs to educate and prevent first and second instances of heart disease and stroke. These state-tailored programs facilitate collaboration among public and private sector partners to help individuals control high blood pressure, lower elevated cholesterol, learn heart disease and stroke signs and symptoms, call 9–1–1, improve emergency response and quality of care, and eliminate treatment disparities. Many of these programs have been successful in reducing risk factors—like high blood pressure.

In fiscal year 2006, only 14 states received funding to implement these prevention programs. The remaining 19 states received funds for planning; which is now largely complete. Because cardiovascular disease remains the No. 1 killer in every state, each state needs basic implementation money for this program. However, current funding levels will not allow for the expansion of this program.

Recommendation.—For fiscal year 2007, the AHA recommends an appropriation of \$8.5 billion plus funding for pandemic influenza preparedness for the CDC, including a 10 percent increase over current funding to return chronic disease preven-

tion to the same level as fiscal year 2002. Within that total, we recommend \$55 million to expand the Heart Disease and Stroke Prevention Program. This funding level would allow the CDC to add up to 4 states to the program, allowing them to conduct a state-tailored plan, and elevate 4 more states from planning to program implementation, maintain the Paul Coverdell National Acute Stroke Registry, and start the development of a state-based cardiac arrest registry.

RESTORE FUNDING FOR THE RURAL AND COMMUNITY ACCESS TO EMERGENCY DEVICES PROGRAM

The Rural and Community Access to Emergency Devices Program provides grants to states to train lay rescuers and first responders to use AEDs and buy and place them where cardiac arrests are likely to occur. During the first year of the program, 6,400 AEDs were purchased and 38,800 individuals were trained. AEDs have been placed in schools, faith-based and recreation facilities, nursing homes, and other locations in communities across our nation.

About 94 percent of cardiac arrest victims die outside of a hospital. Immediate CPR and early defibrillation using an automated external defibrillator (AED) can more than double a victim's chance of survival. Small, easy-to-use AEDs can shock the heart back into normal rhythm. Placing AEDs in more public settings could save thousands of lives each year. Communities with comprehensive AED programs that include training of anticipated rescuers have achieved survival rates of 40 percent or higher.

The Rural and Community Access to Emergency Devices Program is terminated in the President's fiscal year 2007 budget. The budget justification asserts that much of the demand for AEDs has been met, although between fiscal year 2002 and fiscal year 2004 less than half of the grant dollars requested by states for this life-saving program were actually awarded.

Recommendation.—For fiscal year 2007, the AHA recommends that the Subcommittee allocate \$8.927 million for HRSA's Rural and Community Access to Emergency Devices Program to restore funding to its fiscal year 2005 level.

INCREASE FUNDING FOR THE AGENCY FOR HEALTHCARE RESEARCH AND QUALITY (AHRQ)

The AHRQ is a critical partner with the public and private health care sectors. This agency helps develop evidence-based information needed by consumers, providers, health plans and policymakers to improve health care decision making. Through its Effective Health Care Program, AHRQ supports research focusing on outcomes, comparative clinical effectiveness, and appropriateness of pharmaceuticals, devices and healthcare services for a number of conditions, including ischemic heart disease, stroke, and high blood pressure. The new research and comparative effectiveness reviews conducted and funded under this program will help address issues raised in the Institute of Medicine's (IOM) report: *Crossing the Quality Chasm*.

The AHRQ's initiative on health information technology (HIT) is a key element to the nation's strategy to bring health care into the 21st century. This initiative includes more than \$166 million in grants, and through these and other projects, AHRQ and its partners will help to identify challenges to HIT adoption and use, solutions and best practices, and tools that will help hospitals and clinicians successfully incorporate new HIT. To facilitate this effort, the AHRQ's National Resource Center for HIT provides the health care community with technical assistance and consulting services to HIT projects, and particularly focus on addressing challenges to HIT implementation in rural and small community settings.

Recommendation.—The AHA joins with the Friends of AHRQ in advocating for an appropriation of \$440 million for the AHRQ to advance health care quality, cut medical errors and expand the availability of health outcomes information.

INCREASE FUNDING FOR THE CAROL M. WHITE PHYSICAL EDUCATION PROGRAM (PEP)

Physical inactivity is a key risk factor for heart disease and stroke, but Youth Risk Behavior Surveillance data indicates that almost half of 12–21 year olds do not participate in any vigorous physical activity on a regular basis. Despite recent studies by Action for Healthy Kids and the Robert Wood Johnson Foundation showing that almost 80 percent of parents support daily physical education (PE) in schools to help combat physical inactivity and teach life long skills, only 6–8 percent of schools nationally offer daily PE. One of the primary barriers to providing PE is adequate financial resources for equipment, program development, and staff training. The Carol M. White Physical Education Program helps schools overcome this barrier by providing money for school-based physical education activities that teach

life-long physical activity habits. PEP is the only federal program that directly supports PE in schools.

Recommendation.—For fiscal year 2007, the AHA recommends an appropriation of \$100 million for the Carol M. White Physical Education Program. This level of funding will allow the Department of Education to expand the program to more districts while maintaining funding for the duration of previously awarded grants.

Although heart disease, stroke, and other cardiovascular disease are largely preventable, these diseases continue to exact a deadly toll on our nation. As baby boomers age, our nation faces an expanding cardiovascular disease crisis unless significant steps are taken. We urge the subcommittee to consider these recommendations for the fiscal year 2007 budget. Adequate funding of research, treatment and prevention programs will save lives and reduce rising health care costs.

Senator SPECTER. Thank you very much, Dr. Houser.

Senator HARKIN, do you have any comment or question?

Senator HARKIN. Just one. I have a lot of questions for the panel, but just one that I just want to ask Dr. Goldstein. Give us just a few seconds on your view on the potential of stem cell, embryonic stem cell research to benefit juvenile diabetes, type 1 diabetes?

Dr. GOLDSTEIN. We are extremely bullish, Senator Harkin, on the potential to create insulin-secreting cells that are fully functional and respond to glucose. Work has already carried the human embryonic stem cell work to the point of producing endoderm, which is the tissue that then can create the pancreas. Investigators in animal studies can instruct endoderm to make pancreas. If we can make pancreas, that will give us the precursor cells for beta cells and insulin-secreting cells.

So we are extremely, extremely optimistic and wish the work could go forward with full speed.

Senator HARKIN. Thank you.

Senator SPECTER. Senator Shelby, any comment or question?

Senator SHELBY. Yes.

Is anyone on the panel dealing in the autoimmune area, especially dealing with lupus or lupus-related? Dr. Holzman, do you want to comment on where we are going? You heard the first panel earlier.

Dr. HOLZMAN. Actually, in this regard I am more the clinician dealing with patients on the front lines.

Senator SHELBY. That is very important, the clinical work.

Dr. HOLZMAN. I am a nephrologist, a person who deals with kidney disease, and see many of the most complicated patients with lupus and kidney disease. I can tell you first that these are patients who suffer dramatically, that their lives are spent worrying about not only dealing with the current flare, the current problem, but the probability that the disease will recur.

I should say that, thanks to big investments by the NIH in clinical trials, there actually have been some new drugs, drugs that have actually been around for a while but now are proven safer and actually as effective as earlier, more dangerous drugs, such as cyclophosphamide. We are now using microphenalate moftil as a first-line drug for kidney lupus and with I think fairly good success.

Senator SHELBY. So you see a lot of hope there?

Dr. HOLZMAN. I see a lot of hope there. I think that we need to further invest using the latest technology and translational studies in this area.

Senator SHELBY. Thank you.

Thank you, Mr. Chairman.

Senator SPECTER. Thank you, Senator Shelby.

Thank you very much, ladies and gentlemen.

Senator SHELBY. I think Dr. Goldstein was going to say something.

Dr. GOLDSTEIN. Real quickly, Senator Shelby. I would just like to repeat something that Dr. Fauci said: the support of the Immune Tolerance Network, which is a clinical trial translation platform for autoimmune diseases, including lupus, type 1 diabetes, and others. We learn from each other, from the science. Choking that funding off is going to eliminate the possibility to do those cutting edge clinical trials.

Senator SHELBY. Thank you.

Thank you.

Senator SPECTER. Thank you very much, ladies and gentlemen. We very much appreciate your coming in.

We now turn to panel three: Dr. Daniel Koo, Dr. Phil Landrigan, Mr. Emeran Mayer, Dr. Peter McDonnell, Ms. Sandra Raymond, Mr. Herman Taylor, Ms. Suzanne Vogel-Scibilia.

Our first witness is Dr. Daniel Koo, represent the Deaf and Hard of Hearing Alliance, and Dr. Koo is accompanied by an interpreter. Dr. Koo, we begin with you.

STATEMENT OF DANIEL KOO, M.D., ON BEHALF OF THE DEAF AND HARD OF HEARING ALLIANCE

Dr. KOO [speaks through a sign language interpreter]. Mr. Chairman, members of the Subcommittee of Senate Appropriations: On behalf of the member organizations of the Deaf and Hard of Hearing Alliance—

Senator HARKIN. Excuse me. Could you speak into that just a little bit louder. I am having a hard time.

Senator SPECTER. Senator Thurmond always would say: Bring the machine a little closer.

Dr. KOO. Mr. Chairman and members of the Senate Appropriations Subcommittee: On behalf of the member organizations of the Deaf and Hard of Hearing Alliance, a coalition of professional and consumer organizations serving and representing people who are deaf and hard of hearing, it is my pleasure to be here with you this morning to discuss the President's budget request for NIH's National Institute on Deafness and Other Communication Disorders.

My name is Dr. Koo. I am a postdoctoral fellow at Georgetown University conducting neuroimaging studies on language and literacy, supported by NIDCD.

Fiscal year 2007's budget request for NIDCD is \$1.9 million less compared to the fiscal year 2006 appropriation. The DHHA strongly urges Congress not to impose further cuts in NIH or NIDCD research funding and that Congress and the administration work together to ensure appropriate funding that does not compromise current and future research efforts. The DHHA applauds current research being conducted related to people who are deaf and hard of hearing, specifically the strategies to protect hearing, diagnose and prevent hearing loss, and explore genetic modifiers.

However, we urge the NIDCD to continue to pursue and support studies that delve into the acquisition and learning of oral and-or

visual languages, the various communication modes and educational settings.

Cutting the funding most assuredly will prevent the expansion of research in this critical area of need. Funding support for NIDCD to date has allowed many scientists, like myself, to make significant advances in hearing research as well as related sensory and cognitive areas. With congressional support, the NIDCD can continue its important research that aids in preventing hearing loss as well as assisting those who are deaf or hard of hearing.

PREPARED STATEMENT

With hearing loss expected to reach 40 million Americans within the next generation, scientific work taking place at NIH and NIDCD is too critical to the human condition to take a step backward at this time.

Thank you.

[The statement follows:]

PREPARED STATEMENT OF DANIEL KOO

On behalf of the member organizations of the Deaf and Hard of Hearing Alliance, a coalition of professional and consumer organizations serving and representing people who are deaf or hard of hearing, it is my pleasure to be here with you this morning to discuss the President's budget request for the National Institutes of Health, specifically the National Institute on Deafness and Other Communication Disorders (NIDCD).

My name is Daniel Koo. I am a post-doctoral fellow at Georgetown University conducting neuron-imaging studies on language and literacy supported by NIDCD.

The fiscal year 2007 budget request for NIDCD is \$391,556,000, a decrease of \$1,902,000 compared to the fiscal year 2006 Appropriation. The DHHA strongly urges Congress not to impose further cuts in NIH or NIDCD research funding, and we ask that Congress and the Administration work together to ensure appropriate funding to ensure that current and future research efforts are not compromised. With hearing loss expected to affect 40 million within one generation, there has never been a time when research has been needed so much.

The DHHA applauds the current research being conducted related to people who are deaf or hard of hearing, specifically the strategies to protect hearing, diagnose and prevent hearing loss, and explore genetic modifiers. However, we urge NIDCD to continue to pursue and support studies that delve into the acquisition and learning of oral and/or visual languages the necessary precursor to a variety of communication modes and settings. Cutting the funding will most assuredly prevent the expansion of research in this critical area of need.

Funding support for NIDCD to date has allowed many scientists like myself to make significant advances in hearing research, as well as related sensory and cognitive areas that impact the human condition. With Congressional support the NIDCD can continue its important research that aids in preventing hearing loss as well as assisting those who are deaf or hard of hearing. The work taking place at NIH and NIDCD is too critical to the human condition to take a step backward at this time.

Members of the Deaf and Hard of Hearing Alliance include: Alexander Graham Bell, Association for the Deaf & Hard of Hearing, American Academy of Audiology, American Academy of Otolaryngology-Head and Neck Surgery, American Speech-Language-Hearing Association, Conference of Educational Administrators of Schools & Programs for the Deaf, Council of American Instructors of the Deaf, Cued Language Network of America, Deafness Research Foundation, Hearing Loss Association of America, Media Access Group at WGBH, National Association of the Deaf, National Cued Speech Association, Registry of Interpreters for the Deaf, Testing, Evaluation, and Certification Unit, and Telecommunications for the Deaf, Inc.

Senator SPECTER. Thank you very much, Dr. Koo.

We now turn to Dr. Philip Landrigan, representing the Campaign for American Children's Health. Dr. Landrigan.

**STATEMENT OF PHILIP J. LANDRIGAN, M.D., MSc, FAAP, PRESIDENT,
CAMPAIGN FOR AMERICAN CHILDREN'S HEALTH**

Dr. LANDRIGAN. Good morning, Senator Specter, Senator Harkin, Senator Shelby. I'm Philip Landrigan, pediatrician at Mount Sinai Medical School in New York City, and I thank you for inviting me here this morning to come to speak in support of the National Children's Study.

I'd like first of all to thank all of you for the great support that you've given the National Children's Study over the past 6 years since its inception in 2000, and thanks most particularly for the discussion that you had in support of the study just a few minutes ago this morning.

The reason that this Nation needs the National Children's Study is that the children's study will give us information on the preventable environmental causes of the major diseases that afflict American children today—asthma, which has more than doubled; childhood brain cancer has gone up 40 percent; autism, you heard a few minutes ago has gone up remarkably; other learning disabilities.

It's been said that the study is expensive and it is. But the diseases, the chronic diseases that the study will address, cost this Nation more than \$600 billion a year. The very same logic that Dr. Zerhouni invoked this morning when he spoke of the great declines that have been achieved in heart disease because of the Framingham study, the women's health initiative, that same logic applies to the National Children's Study, and it's ironic that I chose to include the same image in my testimony as he used in his screen presentation this morning.

PREPARED STATEMENT

If we fail to fund the National Children's Study it will be a major opportunity lost. The National Children's Study is our generation's best hope, indeed probably our only hope, to get on top of the chronic diseases in America's children.

I thank you.

[The statement follows:]

PREPARED STATEMENT OF PHILIP J. LANDRIGAN

Good morning, Mr. Chairman and Members of the Subcommittee. I am Dr. Philip J. Landrigan. I am a pediatrician, Professor and Chairman of Community & Preventive Medicine, and Professor of Pediatrics at the Mount Sinai School of Medicine. I am Principal Investigator for the Queens, New York Vanguard Center of the National Children's Study. I am also President of the Campaign for American Children's Health, a not-for-profit organization committed to preserving the health of America's children by sustaining the National Children's Study.

Why Do We Need the National Children's Study? The United States needs the National Children's Study because we desperately need the information the Study will provide on preventable causes of the major diseases that confront America's children today. Information from the National Children's Study will provide a blueprint for prevention. The diseases of greatest current concern in American children are:

- Asthma, which has more than doubled in frequency since 1980 and become the leading cause of pediatric hospitalization and school absenteeism;
- Birth defects, which are now the leading cause of infant death. Certain birth defects, such as hypospadias, have doubled in frequency;
- Neurodevelopmental disorders—autism, dyslexia, mental retardation, and attention deficit/hyperactivity disorder (ADHD). These conditions affect 5–10 percent of the 4 million babies born each year in the United States. Reported rates of autism are increasing especially sharply—more than 20 percent per year;

- Leukemia and brain cancer in children and testicular cancer in adolescents. Incidence rates of these malignancies have increased since the 1970s, despite declining rates of mortality. Testicular cancer has risen by 55 percent, and primary brain cancer by 40 percent. Cancer is now the second leading cause of death in American children, surpassed only by traumatic injuries;
- Preterm birth, which has increased in incidence by 27 percent since 1981;
- Obesity and its consequence, type 2 diabetes. Obesity has trebled in prevalence in the United States. Obesity has become common in even the youngest of our children, and for example, 41 percent of 5-year-olds entering kindergarten in the five boroughs of New York City in 2005 were overweight or frankly obese. The future toll of disease and premature death in these youngsters—from diabetes, heart disease, stroke and probably cancer—will be fearsome.

We have a responsibility to safeguard our children. They are the most vulnerable among us, our most precious resource, and the hope for our future. But these rapidly rising rates of chronic disease threaten the health of our children and the future security of our nation.

Indeed, concern is strong among the pediatric community that these rapidly rising rates of disease may create a situation unprecedented in the 200 years of our nation's history, in which our current generation of children may be the first American children ever not to enjoy a longer life span than the generation before them. In other words, if we do not support the necessary research—especially the National Children's Study—and if we fail to take needed preventive action, we are actually at risk of losing hard-won ground in children's health.

What is the National Children's Study?—The National Children's Study is a prospective multi-year epidemiological study that will follow 100,000 American children, a nationally representative sample of all children born in the United States, from conception to age 21. The study will assess and evaluate the environmental exposures these children experience in the womb, in their homes, in their schools and in their communities. It will seek associations between environmental exposures and disease in children. The diseases of interest include all those listed above. The principal goal of the Study is to identify the preventable environmental causes of pediatric disease and to translate those findings into preventive action and improved health care.

The National Children's Study was mandated by Congress through the Children's Health Act of 2000. The lead federal agency principally responsible for the Study is the National Institute of Child Health and Human Development. Other participating agencies include the National Institute of Environmental Health Sciences, the Environmental Protection Agency, and the Centers for Disease Control and Prevention.

By working with pregnant women and couples, the Study will gather an unprecedented volume of high-quality data on how environmental factors acting either alone, or in combination with genetic factors, affect the health of infants and children. Examining a wide range of environmental factors—from air, water, and dust to what children eat and how often they see a doctor—the Study will help develop prevention strategies and cures for a wide range of childhood diseases. By collecting data nationwide the study can test theories and generate hypotheses that will inform biomedical research and the care of young patients for years to come. Simply put, this seminal effort will provide the foundation for children's healthcare in the 21st Century.

The Unique Strengths of the National Children's Study.—Six aspects of the architecture of the National Children's Study make it a uniquely powerful tool for protecting the health of America's children:

1. *The National Children's Study is prospective in its Design.*—The great strength of the prospective study design is that it permits unbiased assessment of children's exposures in real time as they actually occur, months or years before the onset of disease or dysfunction. Most previous studies have been forced to rely on inherently inaccurate retrospective reconstructions of past exposures in children who were already affected with disease. The prospective design obviates the need for recall. It is especially crucial for studies that require assessments of fetal and infant exposures, because these early exposures are typically very transitory and will be missed unless they are captured as they occur.

2. *The National Children's Study Will Employ the Very Latest Tools of Molecular Epidemiology.*—Molecular epidemiology is a cutting-edge approach to population studies that incorporates highly specific biological markers of exposure, of individual susceptibility and of the precursor states of disease. Especially when it is embedded in a prospective study, molecular epidemiology is an extremely powerful instrument for assessing interactions between exposures and disease at the level of the individual child.

3. *The National Children's Study Will Incorporate State-of-the-Art Analyses of Gene-Environment Interactions.*—Recognition is now widespread that gene-environment interactions are powerful determinants of disease in children. These interactions between the human genome and the environment start early in life, affect the health of our children, and set the stage for adult disorders. The heroic work of decoding the human genome has shown that only about 10–20 percent of disease in children is purely the result of genetic inheritance. The rest is the consequence of interplay between environmental exposures and genetically determined variations in individual susceptibility. Moreover, genetic inheritance by itself cannot account for the sharp recent increases that we have seen in incidence of pediatric disease.

4. *The National Children's Study Will Examine a Nationally Representative Sample of American Children.*—Because the 100,000 children to be enrolled in the Study will be statistically representative of all babies born in the United States during the five years of recruitment, findings from the Study can be directly extrapolated to the entire American population. We will not need to contend with enrollment that is skewed by geography, by socioeconomic status, by the occurrence of disease or by other factors that could blunt our ability to assess the links between environment and disease.

5. *Environmental Analyses in the National Children's Study will be conducted at the Centers for Disease Control and Prevention.*—The CDC laboratories in Atlanta are the premier laboratories in this nation and the world for environmental analysis. Because the testing will be done at CDC it will be the best available, and the results will be unimpeachable.

6. *Samples Collected in the National Children's Study Will be Stored Securely and Will be Available for Analysis in the Future.*—New tests and new hypotheses will undoubtedly arise in the years ahead. Previously unsuspected connections will be discovered between the environment, the human genome and disease in children. The stored specimens so painstakingly collected in the National Children's Study will be available for these future analyses.

The Current State of the National Children's Study.—Congress has already laid a firm foundation for the National Children's Study. Between 2000 and 2005, the Congress invested more than \$55 million to design the study and begin building the nationwide network necessary for its implementation.

Seven Vanguard Centers and a Coordinating Center were designated in 2005 at sites across the nation—in Pennsylvania, New York, North Carolina, Wisconsin, Minnesota, South Dakota, Utah and California—to test the necessary research guidelines—with plans to expand the program to 38 states and 105 communities nationwide.

The tough job of designing and organizing is nearly complete. Funding for the Study this year will permit researchers to begin achieving the results that will make fundamental improvements in the health of America's children.

To abandon the Study at this point would mean forgoing all of that dedication, all of that incredible effort, and all of the logistical preparation.

The Study Will More Than Pay for Itself.—The National Children's Study will yield benefits that far outweigh its cost. It will be an extraordinarily worthwhile investment for our nation, and it can be justified even in a time of fiscal stress such as we face today.

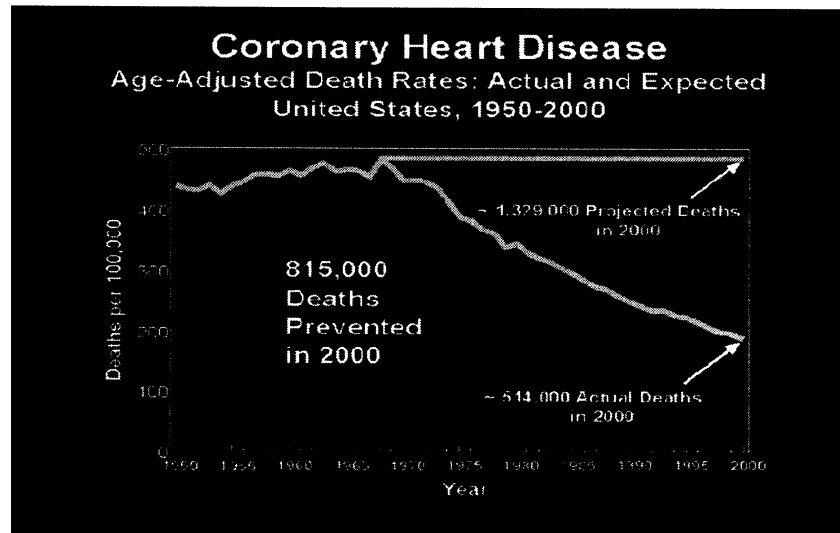
Six of the diseases that are the focus of the Study (obesity, injury, asthma, diabetes, autism and schizophrenia) cost America \$642 billion each year. If the Study were to produce even a 1 percent reduction in the cost of these diseases, it would save \$6.4 billion annually, 50 times the average yearly costs of the Study itself.

But in actuality, the benefits of the National Children's study will likely be far greater than a mere 1 percent reduction in the incidence of disease in children. The Framingham Heart Study, upon which the National Children's Study is modeled, is the prototype for longitudinal medical studies and the benefits that it has yielded have been enormous.

The Framingham Study was launched in 1948, at a time when rates of heart disease and stroke in American men were skyrocketing, and the causes of those increases were poorly understood. The Framingham Study used path-breaking methods to identify risk factors for heart disease. It identified cigarette smoking, hypertension, diabetes, elevated cholesterol and elevated triglyceride levels as powerful risk factors for cardiovascular disease. These findings contributed powerfully to the 42 percent reduction in mortality rates from cardiovascular disease that we have achieved in this country over the past 5 decades (see Figure, next page).

The data from Framingham have saved millions of lives—and billions of dollars in health care costs. The National Children's Study, which will focus on multiple childhood disorders, could be even more valuable.

The Health Benefits of the Framingham Heart Study



The National Children's Study will Yield Benefits in the Near-Term Future.—We do not need to wait 21 years for benefits to materialize from the National Children's Study. Valuable information will become available in a few years' time, as soon as the first babies in the Study are born.

Consider, for example, data on premature births. The rate of U.S. premature births in 2003 was 12.3 percent, far higher than the 7 percent rate in most western European countries. Hospital costs associated with a premature birth average \$79,000, over 50 times more than the average \$1,500 cost for a term birth. Just a 5 percent reduction in rates of prematurity would cut hospital costs by \$1.6 billion annually. Within just two years, that savings would match the full cost of the Study.

The Study Enjoys Broad Support.—The Study enjoys a broad group of supporters, including The American Academy of Pediatrics; Easter Seals; the March of Dimes; the National Hispanic Medical Association; the National Association of County and City Health Officials; the National Rural Health Association; the Association of Women's Health, Obstetric and Neonatal Nurses; United Cerebral Palsy; the Spina Bifida Association of America; and the United States Conference of Catholic Bishops, just to name a few. This broad and diverse group recognizes the overwhelming benefits this Study will produce for America's children.

Congress Should Fully Fund the National Children's Study.—Congress first authorized the National Children's Study in 2000, and has appropriated \$55 million since then to design the Study, complete preparatory research, and designate the seven Vanguard sites that will conduct preliminary testing.

This has been a wise investment that should not be abandoned just as the Study is about to bear fruit. Unfortunately, the Administration has not provided continued funding in the fiscal year 2007 budget, a decision which threatens to squander the investment already made and to throw away the multi-generational benefits the Study will yield.

Funding for the Study this year requires a commitment of \$69 million. These funds will be used to begin enrolling children in the study. They will enable the NIH to continue establishing the 105 study sites around the country. We urge Congress to fully fund the National Children's Study. It is an investment in our children—and in America's future.

The National Children's Study will give our nation the ability to understand the causes of chronic disease that cause so much suffering and death in our children. It will give us the information that we need on the environmental risk factors and the gene-environment interactions that are responsible for rising rates of morbidity

and mortality. It will provide a blueprint for the prevention of disease and for the enhancement of the health in America's children today and in the future. It will be our legacy to the generations yet unborn.

Thank you. I shall be pleased to answer your questions.

Senator SPECTER. Thank you very much, Dr. Landrigan.

We now turn to Dr. Emeran Mayer, representing the Digestive Disease National Coalition. Dr. Mayer.

STATEMENT OF EMERAN A. MAYER, M.D., ON BEHALF OF THE DIGESTIVE DISEASE NATIONAL COALITION

Dr. MAYER. Thank you, Senators Specter, Harkin, and Shelby, for this opportunity. I'm here on behalf of the Digestive Disease National Coalition, representing the International Foundation for Functional Gastrointestinal Disorders. I'm a gastroenterologist and director of an NIH-funded research center at UCLA dedicated to the study of functional gastrointestinal disorders.

These disorders, specifically irritable bowel syndrome, or IBS, are the most common GI disorders in society. They're characterized by chronic abdominal pain and discomfort and affect women disproportionately. IBS's health care costs are \$2 billion annually and exceed \$20 billion when indirect costs are included. Yet the cause of this disorder remains incompletely understood.

During the past 10 years, NIDDK has helped advance biomedical research in the field, bringing us within reach for the first time of several IBS treatments with great potential. The NIDDK is embarking on a strategic planning process for digestive diseases in which IBS will be a critical component. This is essential to advance our understanding, improve treatments, and recruit new investigators for the disease.

The President's proposed cuts to NIH will have a detrimental impact on research advancements in digestive diseases and specifically in IBS. Such cuts would slow our understanding of pathophysiological mechanisms and effective treatments, slow or eliminate pivotal clinical trials, and prevent the pharmaceutical industry to develop new treatments, and most importantly reduce the number of established investigators and send a shock wave to young investigators considering entering into this field.

PREPARED STATEMENT

It is therefore essential to continue our investment into these programs that hold such promise at this point. I urge you therefore to prevent the proposed NIH budget cuts and to prevent the likely unraveling of all the progress that has been made during the past decade.

Thank you for the opportunity to testify.

[The statement follows:]

PREPARED STATEMENT OF EMERAN A. MAYER

Chairman Specter and members of the Subcommittee, thank you for the opportunity to present testimony before you today on the effect that the President's fiscal year 2007 budget for the National Institutes of Health (NIH) will have on functional gastrointestinal and motility disorders research. My name is Dr. Emeran A. Mayer and I am here today representing the International Foundation for Functional Gastrointestinal Disorders' (IFFGD) Board of Directors and the IFFGD Advisory Board on behalf of the Digestive Disease National Coalition (DDNC). I am the Director of the UCLA Center for Neurovisceral Sciences & Women's Health (CNS), a

translational research program recently funded by the NIH that is currently viewed as the leading integrated research program in the world in the area of functional digestive disorders.

Functional gastrointestinal disorders, specifically irritable bowel syndrome or IBS, and motility disorders are the most common gastrointestinal disorders experienced in society and are present in about 25 percent of the U.S. population. The impact on the healthcare system and society in general is substantial. These disorders comprise about 40 percent of gastrointestinal problems for which patients seek health care and the frequency of work absenteeism as a result of these disorders is second only to the common cold. IBS health care costs to society are \$2 billion annually and exceed \$19 billion when indirect factors such as loss of work and productivity are considered. Although the cause of IBS is incompletely understood, we do know that this disorder needs a multidisciplinary approach in research and often treatment, in order to help the millions of patients suffering across the country.

New knowledge on the mechanisms of these disorders, in particular in terms of dysregulation of the elaborate interactions between the nervous system and the digestive system, has resulted in neurophysiological and neuropharmacological investigations which have the potential to produce new pharmaceutical agents as well as disease management programs for treatment of these disorders.

The National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) has been supporting research into the basic and translational mechanisms of functional GI disorders including IBS, in terms of individual research grants (R-01), career development grants to young investigators (K awards), and major support of two research centers, including our own at UCLA. These efforts during the past 10 years have been essential in advancing biomedical research in the field and, for the first time, bringing us within reach of several novel pharmacological treatments with great potential for IBS. The NIDDK is in the process of embarking on a strategic planning process for digestive diseases, and IBS will be a critical component of this plan. Strategic planning is essential to advancing our understanding of this disease, determining improved treatment options for IBS sufferers, and assisting in the recruitment of new investigators to conduct IBS research.

Cutting the budget for the NIH, as is proposed in the President's fiscal year 2007 budget, will have a detrimental impact on the research advancements in this important disease area that have been accomplished during the past several years. Specifically, such cuts would have an immediate impact in the following areas:

- It will slow the elucidation of pathophysiological mechanisms and identification of novel targets, which will have a ripple effect on drug development by the pharmaceutical industry. There will be no new drug development without NIH funded basic and translational research.
- It will slow or eliminate the execution of pivotal clinical trials of novel treatments for IBS.
- Most importantly, it will slow strategic planning and reduce the number of young investigators dedicated to the field by starting an exodus of such individuals into jobs in the pharmaceutical industry and private practice. Such a reduction in the research base will take years to undo.

Biomedical research, sponsored by the NIH, has advanced our understanding of countless diseases and disorders. It is important to continue our investment in these vital programs that hold such promise for our nation's future. Therefore, we ask you to provide an increase of 5 percent in fiscal year 2007 for the National Institute of Diabetes and Digestive and Kidney Diseases and for the NIH overall.

Senator SPECTER. Thank you, Dr. Mayer.

Our next witness is Dr. Peter McDonnell, representing the National Alliance for Eye and Vision Research. Dr. McDonnell.

STATEMENT OF PETER McDONNELL, M.D., ON BEHALF OF THE NATIONAL ALLIANCE FOR EYE AND VISION RESEARCH

Dr. McDONNELL. Thank you, Chairman Specter, Senator Harkin, Senator Shelby.

The President's proposed fiscal year 2007 budget would cut National Eye Institute funding by 0.8 percent, or \$5.3 million. This will have a significant detrimental impact on the entire NEI research portfolio, especially research programs into age-related macular degeneration, AMD. As Dr. Zerhouni mentioned this

morning, this is the leading cause of blindness now in the United States. It robs our seniors of their independence.

I offer three examples. The NEI has identified variants of a gene associated with the body's inflammatory response responsible for 50 percent of the risk of developing AMD. Without adequate funding, NEI will not be able to develop diagnostics for early detection of at-risk individuals and conduct clinical studies with promising therapies, as well as study the impact of the inflammatory response and other degenerative eye diseases.

The NEI has demonstrated that dietary zinc and anti-oxidant vitamins actually reduce vision loss in individuals at risk of developing AMD. Without adequate funding, NEI will not be able to proceed with follow-up clinical studies to identify additional dietary supplements used singly or in combination to demonstrate even greater protective effects against progression to advanced disease.

NEI's research has resulted in the first generation of FDA-approved drugs to treat abnormal blood vessel growth in the wet form of AMD, halting further vision loss. NEI's ability to conduct clinical studies of these therapies in patients with macular edema associated with diabetes and diabetic retinopathy would also be jeopardized.

Thank you, Mr. Chairman, and we appreciate the subcommittee's efforts to increase NIH and NEI funding in the fiscal year 2007 budget.

Senator SPECTER. Thank you very much, Dr. McDonnell.

We now turn to Ms. Sandra Raymond, representing the Lupus Foundation of America.

STATEMENT OF SANDRA RAYMOND, ON BEHALF OF THE LUPUS FOUNDATION OF AMERICA

Ms. RAYMOND. Good morning, Mr. Chairman, Senator Harkin, Senator Shelby.

Lupus is the prototypical autoimmune disease, so an investment in lupus research may in fact produce answers to many other autoimmune diseases affecting more than 23 million Americans. In recent years, NIH has had funded studies that give us great hope that we are on the brink of major breakthroughs in lupus research.

For example, one study, an adult stem cell transplantation study, is carried out on only the most severely ill of lupus patients, for whom all other treatments have failed. Fifty percent of these patients having the procedure had disease-free survival for 5 years.

In another NIH-funded study, researchers identified a gene that plays a role in one of the immune system pathways meant to fight infection. In people with lupus, this pathway turns on, but never turns off.

Mr. Chairman, should NIH appropriations be curtailed there may not be a future generation of scientists to do lupus research. Already the hint that funding may be reduced has caused leaders in our field to consider better funded areas. Cuts in NIH funding could bring to a standstill support of clinical trials and large observational studies in lupus and could limit research on those at highest risk for lupus, women of color.

PREPARED STATEMENT

NIH-funded research currently in progress will lead to new and improved treatments for lupus. There has not been a new FDA-approved drug for lupus in almost 40 years and the drugs that our patients are currently taking are very harsh chemotherapies, chemotherapies in lupus as well as in cancer.

Thank you.

[The statement follows:]

PREPARED STATEMENT OF THE LUPUS FOUNDATION OF AMERICA, INC.

I am Dr. Michael Madaio, Chief of Nephrology, Professor of Medicine, Temple University School of Medicine and a lupus researcher. The Lupus Foundation of America, Inc. (LFA) appreciates the opportunity to submit written comments for the record regarding funding for lupus related programs for fiscal year 2007. The LFA is the nation's leading non-profit voluntary health organization dedicated to improving the diagnosis and treatment of lupus, supporting individuals and families affected by the disease, increasing awareness of lupus among health professionals and the public, and finding the causes and cure. As you may know, lupus is a debilitating, chronic autoimmune disease that causes inflammation and tissue damage to virtually any organ system; it can cause significant disability or even death. Lupus is the prototypical autoimmune disease; therefore, finding answers to questions about lupus may also provide understanding about other autoimmune diseases that affect 22 million Americans. The leaders and members of the LFA and the 1.5 to 2 million people suffering from lupus respectfully request for fiscal year 2007 \$29.7 billion for the National Institutes of Health (NIH) to support lupus research. Specifically, we urge Congress to direct NIH to support and bolster lupus research across all relevant institutes, centers, and offices.

I have been funded for lupus research for over 20 years. I am proud to be affiliated with the Lupus Foundation of America as a member of the Medical Scientific Advisory Board and Chairman of the Medical Advisory Board for the Southeastern Pennsylvania Chapter of the LFA. While I am a nephrologist, since my research and clinical practice is focused on lupus, I really work day-to-day within the realms of nephrology and rheumatology as well as other medical specialties and subspecialty areas. I understand the importance of biomedical research funding and the impact that federal research funding has had, does have, and can have on the lives of the 1.5 million people living with lupus and the 22 million Americans with other autoimmune diseases.

After a tragic 40 year dearth of new treatments to manage this often debilitating and devastating disease, the good news is that we finally are on the brink of major breakthroughs, thanks to research sponsored by the National Institutes of Health. Exciting research and strides in treatments for people with lupus are on the horizon and a sustained investment now in lupus research will speed the day to better treatments and a cure. One exciting study, adult stem cell transplantation, was carried out on only the most severely ill of lupus patients for whom all other treatments have failed. Fifty percent of the patients having the procedure had disease free survival at 5 years. In another NIH funded study researchers identified a gene that plays a role in one of the immune system pathways meant to fight infection. In people with lupus this pathway turns on and never turns off. These findings and others will lead to effective ways of treating lupus and other autoimmune diseases affecting 23 million Americans.

Specifically, I am conducting extensive research on lupus nephritis, which is kidney involvement in lupus disease. My field is advancing rapidly, due in large part to factors directly dependent on NIH funding:

- the burgeoning growth in the number of new animal models, including a wealth of informative transgenic and gene-targeted mutants;
- increased access to improved powerful technologies such as gene and protein arrays, now available at many institutions and to many investigators through NIH core facilities;
- new technologies that permit successful query of the very small amounts of human tissue typically available from patients and, collaboration across disciplines and across institutions to bring crucial expertise together;
- new insights into underlying biology and pathophysiology in immunity and lupus are constantly emerging;
- technologies to identify biomarkers are improved and accessible; and

—new approaches to therapy are being explored.

These endeavors are bearing fruit but they are highly dependent on NIH funding. If funding for the NIH is cut or level funded, it could cripple or paralyze current lupus research efforts.

As lupus is a systemic disease that can affect any organ or tissue elucidating pathogenesis (or cause) and treatments of lupus will have direct impact on many other autoimmune diseases (e.g. results and treatments translating to other diseases). Providing adequate resources to support lupus research will help the nation turn the corner on finding better treatments or a cure for lupus while also supporting breakthroughs and progress for other disease states. It is important to note that the corollary is true: cuts in lupus research funding also will have an adverse effect on progress for lupus and for progress in related diseases. Cuts in NIH funding could bring to a standstill support of clinical trials and large observational studies, and could curtail research on those at highest risk for lupus, women of color; it also could negatively impact pediatric research at a time when researchers have just begun to undertake studies in important new areas. Furthermore, insufficient federal funding also could slow much-needed genetic research when we are just discovering the critical components that may contribute to lupus and its effects. Therefore, it is critical that biomedical researchers be provided the necessary resources to continue seeking answers to the questions that will lead to better lupus treatments. Increased research funding will help deliver much-needed breakthroughs from the laboratory to patients in need.

The National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS), the institute most involved in lupus research, is one of the smallest institutes at NIH. In the past 2 years there has been a decrease in research funding for NIAMS overall, with a 10 percent decrease in new research grants. Currently, only 12–15 percent of the grant applications submitted to NIAMS receives funding. Further cuts will cause this rate to drop precipitously to below 10 percent next year. Just 2 or 3 years ago, funding levels were at 25–30 percent. Cuts in research funding, coupled with the rate of biomedical research inflation (3–4 percent per year), further erode NIAMS' ability to fund lupus research grant applications at the rate necessary to begin making real progress. As such, an increase above the rate of biomedical research inflation is necessary to allow NIH to sustain and build on its research progress resulting from the recent budget doubling while avoiding the severe disruption to that progress that would result from a lesser increase or cut.

Furthermore, in the proposed budget for NIAMS for 2007 there will be a loss of 10 training grants; each grant funds training for four physicians, mostly rheumatologists. Young and senior investigators alike are moving into other fields because of the lost of funding. Exacerbating the situation, medical schools are struggling financially due to public funding cuts thus eliminating any safety net for researchers that may have previously existed. As a result, young investigators are not attracted to lupus research which means there will be not be a future generation of lupus scientists and clinicians to do research. Moreover, after having attracted scientists to translational immunology in the last 5 to 10 years, when funding was increasing, there is now a possibility we could lose both the current and next generation of young investigators. Increased funding is necessary to support an adequate number of training grants. Without research and training funds lupus researchers might be forced to become private practice physicians instead, leading to an imbalance in the health care system: sufficient numbers of physicians to treat lupus patients, but no new treatments with which to care for them, and no researchers to develop the cures of tomorrow.

We recognize and appreciate that Congress and the nation face unprecedented fiscal challenges; however, we cannot afford to lose ground in biomedical research at such a promising time. The LFA looks forward to working with the subcommittee and others in Congress to reduce and prevent the suffering caused by lupus. We stand ready to serve as a resource for any information you may need in this regard and thank you for this opportunity to submit written testimony for the record concerning fiscal year 2007 lupus related funding.

Senator SPECTER. Thank you very much, Ms. Raymond.

Our next witness is Dr. Herman Taylor, representing the Jackson Heart Study. Dr. Taylor.

STATEMENT OF HERMAN A. TAYLOR, JR., M.D., ON BEHALF OF THE JACKSON HEART STUDY

Dr. TAYLOR. Thank you, Mr. Chairman, and good morning, Senator Harkin, Senator Shelby. I am Herman Taylor, professor and

cardiologist at the University of Mississippi Medical Center and also with appointments at Jackson State and Taluga College.

I am proud this morning to come to you on behalf of the largest study of cardiovascular disease ever undertaken in the African American population. It is called the Jackson Heart Study. The NHLBI and the National Center for Minority Health and Health Disparities are the NIH entities that fund this groundbreaking work. We are not only doing research, but we are actively involved in training young people to be scientific leaders for tomorrow.

We are accomplishing much, but our challenges are huge. A well documented and widening gap has opened up between blacks and other citizens of this country with respect to cardiovascular health. While most Americans have enjoyed a 40-year decline in death rates from cardiovascular disease, there has been virtually no change in the death rate from cardiovascular disease for African Americans in the State of Mississippi and certain other urban areas in other parts of the country share these equally dismal statistics.

So while the Jackson Heart Study is a very heartening and wonderful undertaking, if the intent is to approach these disparities what we have done thus far can be compared to throwing a 10-foot rope to a man at the bottom of a 40-foot well. It is a great idea, it is a good intention, but it comes up short.

PREPARED STATEMENT

If we consider the question of health disparities an important national priority, you have to ask yourself what if we were equal. Dr. David Satcher asked that question in a recent publication and he concluded, looking at CDC statistics, that last year 80,000 African Americans died unnecessary deaths compared to their white counterparts. In our State 1,200, our small southern State, 1,200 African Americans died unnecessarily.

To reverse this trend, we must support research and extend the work of the Jackson Heart Study. Thank you.

[The statement follows:]

PREPARED STATEMENT OF HERMAN A. TAYLOR, JR.

I am proud to come to you today on behalf of the largest and most comprehensive study of CVD in the African American community ever conducted—the JHS. Through the generous support of 2 NIH components—NHLBI and the NCMHD—this ambitious and multifaceted project is emerging as a leading study on CV disease among African Americans. Besides its establishing a growing database of detailed health information and test results ranging from advanced images of the heart to genetics to measures of stress and psychological parameters, the JHS is also an incubator for the scientific leaders of tomorrow through our education and training programs that involve minority students in didactic classroom sessions and practical research experiences. And while we search for answers and train future leaders, we also are taking action NOW—to serve the community with important health information from our study as well as others.

We are relatively new, born during the period of NIH budget doubling, and already we have accomplished much within the Jackson community and beyond. However, despite the promise of the JHS and our optimism over its impact, I come to you with a deep concern, summarized in the arresting quotes below.

“It has been discovered that the health of [blacks] in [parts of] Mississippi is deteriorating while the health standards for the nation are improving . . .”—The Wall Street Journal

“Cardiovascular deaths in MS seem to be rising while they have fallen for the past 30 years for the rest of the country.”—Circulation (the official organ of the American Heart Association)

These 2 quotes are distressing, whether you are African American or not, whether you are Mississippian or not. However, the magnitude of the problem they summarize becomes clearer when you consider that the two statements were made 32 years—a full generation—apart. The notion that in the richest country in the history of man, one location or group within its borders can be so singularly and peculiarly burdened from a largely preventable disease is barely credible. But it is true, and it has the status quo for around forty years.

So while the JHS represents an inspired, timely effort of the NHLBI and the NCMHD, to freeze research efforts at the current levels of funding would be like throwing a 10 foot rope to a man at the bottom of a 40 foot hole. We come up short, and despite the right idea and a noble attempt, the problem of disparate CV health remains unsolved. To extend the reach of the JHS to its full potential, our Study and other complementary studies—and the investigators driving them—must thrive, and have support for their approaches and new ideas.

The JHS contributes to extending the research lifeline in several important ways. First there is the core JHS Study itself. Classically designed in the pattern of the world famous Framingham Study, it offers a chance to Study a wide list of possible causes for poorer cardiovascular health among African Americans, to inform precise interventions that will reduce disparities. Funded through 2013 by NHLBI and NCMHD, it is a landmark undertaking. The JHS also is innovative in its list of partnering institutions. Besides the guidance and support of the NHLBI and the NCMHD, 3 local Jackson Institutions of higher learning take active part in making the JHS work—Jackson State University, University of Mississippi Medical Center, and Tougaloo College all have unique and vital roles in the Study. Comprising a team of 2 Historically Black institutions and a third predominantly minority-serving institution, this combination has been ground-braking and synergistic in the service of this population-based study of an African American population. Training of promising young talent from the affected population and participation of HBCU's in epidemiological research at the highest level is bearing fruit for the Nation in terms of a rising cadre of leaders in the relevant fields.

However, the potential impact of the JHS is bigger than even this important core Study will provide. This is because not only is the JHS a Study in its own right, it is a platform for critical spin-off studies. These “Ancillary Studies” require secondary funding that is NOT a part of the JHS contract funding. A flat or declining NIH budget threatens these important studies, where much of the truly innovative work on health disparities could occur. For instance, nearly all of the genetics studies of heart disease in the JHS require this ancillary funding. The genetics of CVD may be the key in the lock of our understanding of much of the current epidemic. Implications of these studies may be huge for not only African Americans, but all people threatened by the nation's number one killer. Flat budget lines severely limit the opportunities for such important studies. This is especially devastating to new investigators, those who apply for the career development (K) awards that NHLBI has been so committed to funding. These young people are the cadre of scientists in whom we are investing our future hopes of American world leadership in health research, and the ultimate resolution of health disparities.

The future of innovative science from the JHS is therefore tied in important ways to Ancillary studies (R01's) and career development (K) awards for new investigators. Holding the line on the NIH budget is to worsen a palpable threat scientists now feel—that of being squeezed out of a zero-sum game where more and more scientists are fighting each other and the rising cost of research in order to launch and sustain promising careers. This is especially devastating to new investigators, in whom we are investing our future hopes of American world leadership in health research.

Therefore, the JHS at this point in its evolution can be thought of as a major platform for scientific discovery—an incredible growing database that is a national resource. If the growing brain trust of scientists—in Jackson as well as Boston, Bethesda, Minneapolis, Baltimore, New York, Chicago and elsewhere—who are showing active interest, receive funding for meritorious ideas, the JHS stands to produce important breakthroughs in our understanding of the CVD patterns seen in AA and others. However, if flat pay lines prevent the funding of new ideas for using this unparalleled resource, the trajectory of discovery will be blunted, the pace of advance slowed, and important scientific opportunity, squandered. And the wisdom shown by NCMHD and NHLBI in building this platform for discovery will be in many ways betrayed.

We cannot afford to squander any opportunities to improve health overall and eliminate health disparities. I witness the impact of failed promises everyday. Among my patients, I see the end result of our incomplete understanding of heart disease: in young mothers whose hearts fail after childbirth for no good reason—though we have a name for it—peripartum cardiomyopathy—we don't understand it, and we don't understand why it afflicts Blacks more than other Americans. I see it in fathers with no known risk factors, but develop coronary disease anyway. I see it in people suffering from morbid obesity who not only are at increased risk for disease, but because of their size, therapeutic and diagnostic interventions themselves are technically much more difficult. Standard operations are often riskier, and sometimes impossible to perform. With 1,200 unnecessary deaths from CVD among AA in our small Southern state alone, deferring the dream of health equality only adds to our regional tragedy of health disparities. With 80,000 unnecessary deaths nationally among African Americans in 2004 (most from CVD) research retrenchment in the form of flat lining or cutting the research budget only defers finding answers that were needed yesterday for our Nation's health. An act of national compassion and strong resolve is necessary. I pray that this Congress and President will engage this great threat to the dream of a healthy, vigorous nation. It is in our compelling national interest to do so.

Thank you, Mr. Chairman. I would be pleased to answer any questions that the Committee may have.

Senator SPECTER. Thank you very much, Dr. Taylor.

Our final witness is Dr. Suzanne Vogel-Scibilia, representing the National Alliance for Mental Illness.

STATEMENT OF SUZANNE VOGEL-SCIBILIA, M.D., PRESIDENT, NATIONAL ALLIANCE ON MENTAL ILLNESS

Dr. VOGEL-SCIBILIA. Greetings from Beaver County, Pennsylvania, Senator Specter.

I'm a volunteer with—

Senator SPECTER. Whereabouts? Where?

Dr. VOGEL-SCIBILIA. Beaver.

Senator SPECTER. Thank you.

Dr. VOGEL-SCIBILIA. I'm a volunteer at NAMI and the president of the National Alliance on Mental Illness, and I have been a practicing psychiatrist and a family member of persons with mental illness as well as a consumer with bipolar disorder myself. I have had periods of severe illness, but I have had a good recovery.

Unfortunately, though, many people in our country have not yet achieved recovery. If Congress cuts funding at the NIMH as the President has suggested, we will have to continue to have millions of people in this country with chronic disability and a \$40 billion loss in economic productivity each year alone for schizophrenia, not to mention other illnesses.

Because of the past doubling of the research budget, NIMH has brought forth vitally important real world trials to impact the treatment of all persons with schizophrenia, bipolar disorder, and depression. Unfortunately, though, the future gains in medication and treatment options for this vital research will not be realized unless further medical support is given to these important studies. We will be unable to fund the United States whole genome studies for serious mental illness, which could transform the understanding of causes and risk factors for these devastating illnesses and open up new avenues of effective treatment.

Last, we will be unable to advance schizophrenia and bipolar research progress. One example is in the understanding if early intervention and medication therapy and rehabilitation will prevent disability and morbidity for persons with new onset schizo-

phrenia. We will also be unable to address and prevent the epidemic of suicide in this country, including a substantial number of our young people who die or are disabled before their life has truly started, and the elderly who are cheated from their retirement years.

For myself, my children, and the people who belong to over 1,100 affiliates of NAMI in the United States of America, we humbly thank you for all your reform to express our concerns and hope that research dollars will be provided to help those of us who suffer.

Thank you very much.

Senator SPECTER. Thank you very much, Dr. Vogel-Scibilia.

One question, Dr. Taylor. When you say "unnecessary deaths," how would you define that?

Dr. TAYLOR. Yes. The term, sir, refers to deaths that you would not expect, given statistical projections, given the current level of care and our understanding of risk factors for cardiovascular disease. So these are people who—a certain number of people are expected to die, of course, from certain diseases, like heart disease, every year. Well, these are people who you would not expect to have died. Dr. Satcher and others have termed these "unnecessary deaths."

Senator SPECTER. You are saying in effect that that is higher for blacks, African Americans, than others?

Dr. TAYLOR. Senator, it is substantially higher. Again, the national prediction is that 80,000 of these deaths occur from a variety of causes and the lion's share of those deaths are due to cardiovascular causes.

Senator SPECTER. What is the reason for the higher incidence of deaths among blacks?

Dr. TAYLOR. Well, this is the principal focus of the Jackson Heart Study and studies like it, to figure that out. Clearly there are higher levels of risk factors, such as obesity, hypertension, diabetes. But one must ask the question, why are those risk factors higher? We cannot simply say, well, there is more hypertension, therefore we expect more deaths. The question is why is there more hypertension and related problems?

Also, access to care clearly is a major part of this. But historically, African Americans as a group have been understudied with regards to what are the true determinants of poor health. Studies like the Jackson Heart Study and studies related to it I think will help unravel these questions and give us detail that we might not even suspect at this point. The Jackson Heart Study, for instance, includes studies into genetic underpinnings of various illnesses. But on the opposite end perhaps of the spectrum, we look very carefully at psychological determinants of ill health, at social and behavioral parameters that may also impact how well people do in terms of their overall health.

Senator SPECTER. Senator Shelby.

Senator SHELBY. Thank you, Mr. Chairman.

Ms. Raymond, what funding do we really need to sustain research into lupus at NIH in your judgment?

Ms. RAYMOND. Well, presently the amount of funding now allocated is around \$66 million. In order to really sustain and break through, I think we need \$200 million.

Senator SHELBY. That is a lot of money.

Ms. RAYMOND. A lot of money.

Senator SHELBY. But a lot of promise, too.

Ms. RAYMOND. I think so. We have many deaths due to lupus.

Senator SHELBY. Absolutely.

Ms. RAYMOND. It is a fatal disease. It is prototypical because it affects any organ system, any tissue system in the body.

Senator SHELBY. 90 percent of them are women, are they not?

Ms. RAYMOND. 90 percent are women and a majority are women of color, African American, Hispanic, Asian, and Native Americans.

Senator SHELBY. Dr. McDonnell, macular degeneration. What is the real promise once you are diagnosed in that area?

Dr. MCDONNELL. Well, Senator, this is now with the tidal wave of aging Americans, this has taken over from diabetes as the major cause of Americans to go blind. It is a progressive disease involving—it is almost our Alzheimer's or Parkinson's—a neurodegenerative condition of the cells of the retina, of the back of the eye. The eye is part of the brain, and this progression occurs.

Now we believe we have some dietary supplements that may slow the progression.

Senator SHELBY. What are these?

Dr. MCDONNELL. Anti-oxidant vitamins and zinc have been shown, thanks to an NEI-funded study, to delay the progression to severe forms of the macular degeneration. Now, we have some treatments that can treat severe forms with blood vessels that are causing leakage and bleeding and scarring in the back of the retina. We also hope to be able to begin and expand upon studies of regenerative medicine using stem cells, such as would be done in other fields, to restore the cells that are lost or damaged from this disease.

Senator SHELBY. So there is great promise everywhere in biomedical research. It has just got to be properly funded. Is that the bottom line?

Dr. MCDONNELL. I agree with that. As you heard, lupus also damages the eye. The eye is part of the brain. Fortunately, not all patients are afflicted in the eye, but we have patients go blind and we need the same treatments that would improve the kidney damage and brain damage of lupus also for our eye patients.

Senator SHELBY. Thank you.

Mr. Chairman, thank you.

Senator SPECTER. Thank you, Senator Shelby.

Senator Harkin.

Senator HARKIN. Thank you, Mr. Chairman.

Dr. Landrigan, thank you for bringing up the children's study. That is why I brought it up earlier. You talked about the benefits to children, but would it not also benefit adults also? I mean, obviously obese children have later complications as they grow older. Many of the things that happen to you in childhood you carry with you, especially mental health. If you have mental health problems early in life and they are not attended to, it can manifest itself later on.

So I just wanted to draw you out a little bit on that in terms of the benefits of the children's study, not just to kids, but I think across the spectrum.

Dr. LANDRIGAN. Yes, Mr. Harkin, that is absolutely true. There is an expanding body of research, called the early origins of adult disease hypothesis. For example, slow fetal growth of the baby still in the mother's womb is associated in young adult life with an increased risk of diabetes, hypertension, and heart disease. There are some intriguing clues, more from animal studies than human at the moment, that early exposures to toxic chemicals may cause brain damage that does not become manifest in childhood, but shows up four, five, six decades later in the form of dementia or Parkinson's disease.

So I think it is both to protect America's kids as well as future generations of adults that we are seeking the full funding for the study to be restored in fiscal year 2007, which would be \$69 million, and also assurances that the study will continue to be funded in the years ahead. It will not succeed unless the funding for it is sustained.

Senator HARKIN. Thank you very much.

Mr. Chairman, I do not have any further questions. I would just again for the record state, Mr. Chairman, that you and I and others on this committee had planned for this children's study. It was passed in 2000. A lot of planning went into this and forethought went into it to set up this long-term study, and I just cannot believe that we are just going to just stop it at this point in time.

So we have just got to do everything we can to mandate, if we have to, mandate—I do not know if there is anyone here from OMB, but mandate—that this funding go forward this next year.

Thank you very much.

Senator SPECTER. Thank you. Thank you, Senator Harkin.

I thank all of you. We are fighting. We put up a Specter-Harkin amendment and added \$7 billion to the budget in the Senate. Unfortunately, that has not been accomplished in the House. We have added from that \$7 billion \$2 billion for the National Institutes of Health.

But this is a battle that really has to be engaged in by 110 million Americans who are suffering directly or indirectly from the kinds of illness which we have heard about here today.

We thank you for coming in. This has been an impressive hearing because it puts a face on these ailments. They are sort of abstractions. They are not abstractions if your wife is suffering from them or a close relative or a close friend or you are suffering from them. They are not abstractions at all. But there has to be a very intense advocacy effort. We call it lobbying around here. It is really advocacy. Your organizations are very, very important in this advocacy effort. We thank you for what you are doing. But you have to contact your counterparts everywhere.

The amendment which Senator Harkin and I sponsored won 73 to 27, but there were 27 Senators who voted no and you ought to identify them and you ought to march on them in their cities, in their States, seriously, very, very seriously. It is a little hard, with all that Senator Harkin and I have to do—he has got to bounce out of here and go to Iowa for a meeting later today and I have got

to conduct a hearing on campus violence in Philadelphia at 2 o'clock. I have not been in my office all week. I have been on the floor managing the immigration bill. Before that I was fully occupied with the Supreme Court nominations.

But your groups are advocates and I would like to see that million person march. But it has got to be done. We are a democracy and people in Washington pay attention to people in their home States. If I get seven letters, I have got 12 million constituents, I think it is significant. You have really got to be more politically active, not Democrat or Republican active, but active for these issues, active for NIH, active for stem cells.

I am convinced there are cures for all of these ailments and we have the resources to do it. It is a question of how many doctors and hospitals and research scientists and dedicated people you have. It is not a matter of how many dollars you have. It is a matter of what your resources are. The money flow comes out of Washington to a large extent, also out of your State capitals.

ADDITIONAL COMMITTEE QUESTIONS

There will be some additional questions which will be submitted for your response in the record.

[The following questions were not asked at the hearing, but were submitted to the Department for response subsequent to the hearing:]

QUESTIONS SUBMITTED BY SENATOR ARLEN SPECTER

LIVER DISEASE RESEARCH BRANCH

Question. Dr. Zerhouni, 3 years ago, the NIDDK established a Liver Diseases Research Branch within its Division of Digestive Diseases and Nutrition. Please explain the benefits of having a Research Branch dedicated to a specific area of research and describe how this Liver Disease Research Branch has succeeded in its mission.

Answer. Research on diseases of the liver is a trans-NIH effort involving 19 institutes, centers, and offices. The National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) has lead responsibility for liver disease research at the NIH. Within the NIDDK, liver disease research is under the purview of the Division of Digestive Diseases and Nutrition. The Federal liver disease research effort has benefited greatly from the establishment in 2003 of an organizational entity within the NIDDK—the Liver Disease Research Branch—dedicated exclusively to this very important area. This new Branch was formed to focus and coordinate research efforts on critical areas relevant to liver and biliary disease, such as hepatitis and liver transplantation.

Following a national search, Jay H. Hoofnagle, M.D., an internationally recognized authority in liver disease research, was appointed as Chief of this Branch. The NIDDK recruited an additional scientific Program Director with expertise in liver diseases to further support the efforts of the Branch. The Branch also includes scientific experts in the areas of viral hepatitis, clinical trials, epidemiology and data systems, genetics and genomics, and research training and career development.

The Liver Disease Research Branch has accelerated research on liver disease supported by the NIDDK and has helped to coordinate and stimulate liver-related research efforts across the NIH and within other Federal agencies, such as the Centers for Disease Control and Prevention, the Department of Defense, the Bureau of Prisons, the Food and Drug Administration, and the Department of Veterans Affairs. An initial important task set for the Branch was to prepare the trans-NIH Action Plan for Liver Disease Research. The Plan provides an overview of the current burden of liver disease in the United States, the current level of NIH research funding in liver disease, and recent research advances. Importantly, the Plan also summarizes challenges to advancing liver disease research and delineates the major goals for future research. Specific goals for the next 10 years are defined for each of 16 topic areas in liver disease research.

One mission of the Branch is to oversee the conduct of the Plan, which includes annual Progress Reviews to aid in its implementation through an ongoing assessment of progress and the need for further efforts to promote liver and biliary disease research. The Progress Review for 2005, the first year following release of the Action Plan, is available at: http://www.niddk.nih.gov/fund/divisions/ddn/ldrb/Progress_reviews.htm. The Branch also develops and coordinates future NIH efforts in liver disease research aimed at reaching the goals defined in the Plan.

Thus, the Branch is succeeding in its mission to plan and direct the NIH program of liver research, as evidenced by an impressive array of initiatives that include major clinical trials and special program announcements in the areas of proteomics of the liver, biomarkers for liver disease, non-invasive tests for diagnosis and staging of liver disease, and ancillary studies linked to specific clinical trials, databases and cohort studies on liver disease (<http://www.niddk.nih.gov/fund/program/DDN-list.htm#Liverprograms>).

UROLOGY RESEARCH STRATEGIC PLANNING

Question. Our conference report last year “urged the NIDDK to continue to support and develop the ‘Urologic Diseases in America’ report and to include urological complications as well as diabetes and obesity research initiatives.” This language was included in response to concern that the NIH-wide Obesity Strategic Plan did not address urological issues such as, stress urinary incontinence or erectile dysfunction (ED), two conditions highly associated with obesity. These conditions severely affect quality of life and result in high medical costs. How do you ensure that all disciplines are represented in strategic planning?

Answer. The NIH acts to ensure that its strategic planning efforts for research are comprehensive, inclusive, and evidence-based. Currently, strategic planning is conducted by the individual Institutes, Centers, and Offices of the NIH, as well as through trans-NIH and interagency mechanisms, as appropriate. The NIH Office of Portfolio Analysis and Strategic Initiatives, which I established recently, will have an instrumental role in facilitating both individual and trans-NIH strategic planning efforts through its planned activities.

To ensure effective planning processes, the NIH seeks input from a wide array of stakeholders, including scientific experts, representatives from professional organizations, and patient advocates. For example, most strategic planning for urologic diseases research is conducted by the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK). In two major planning efforts, the NIDDK assembled large, multidisciplinary groups of scientists and medical professionals prominent in their fields and active in patient and professional societies related to bladder disease in 2002, and in pediatric urology in 2006. These groups were thus able to bring multiple perspectives to bear when reviewing progress in bladder disease and pediatric urology research, and to provide broad-based assessments of research needs and recommendations for future action, including recommendations regarding the impact of obesity and diabetes on certain urologic diseases. As a result, these groups’ 2002 and 2006 reports have served as a model for NIH planning for urologic diseases research and for trans-NIH collaborations in this area. Moreover, the NIDDK has continued to gather multidisciplinary expert groups to assist in more focused areas of research planning, such as prostate disease, and urologic diseases in women. All of these efforts are bolstered by the Urologic Diseases in America report, which has provided significant information related to major urologic diseases. The NIDDK is strongly committed to maintaining this program, and a research solicitation is being developed for the next phase of Urologic Diseases in America that will include assessment of the impact of diabetes and obesity on urologic diseases. Additional, ongoing assessments of research progress in urologic diseases through advisory group meetings, scientific conferences, and stakeholder input allow flexibility, capitalization on new research advances, and the opportunity to strategically address research gaps and barriers that may emerge or become evident over time.

The Strategic Plan for NIH Obesity Research, developed by the NIH Obesity Research Task Force, similarly drew upon a broad base of scientific expertise within and external to NIH. The plan focuses, in part, on goals and strategies to break the link between obesity and its associated health conditions. Recommendations from this and other plans and from ongoing strategic planning efforts are reflected in NIH action. For example, the NIDDK has funded the Program to Reduce Incontinence by Diet and Exercise (PRIDE) study, which is examining the impact of weight loss on urinary incontinence in overweight and obese women. The benefits of considering multiple disciplines in research planning can be seen in research results. For example, the NIH-funded Diabetes Prevention Program recently found that weight loss improves bladder control in women with prediabetes. This new knowledge, that

an intervention proven to reduce risk of type 2 diabetes can also reduce episodes of urinary incontinence, has the potential to improve health and quality of life for the large number of older American women who have both prediabetes and bladder control problems. The NIH has also been supporting a similar study in patients with type 1 diabetes who are participating in the Epidemiology of Diabetes Interventions and Complications study, to determine whether intensive control of blood sugar levels—an intervention proven to reduce risk of developing eye, kidney, nerve, and cardiovascular complications of diabetes—also reduces risk of urologic complications.

OPASI TRANS-NIH FUNDING PROGRAM

Question. Dr. Zerhouni, you have initiated a new trans-NIH funding program, which requires each Institute and Center to contribute a fixed portion of their appropriations for cross-cutting research initiatives. Can this program move forward as planned in an environment of no real increases in NIH funding?

Answer. The Administration has focused resources on our highest priority: protecting the citizens and our homeland. This underscores the importance of being as strategic as possible with NIH dollars to catalyze high-impact research. The time is right for NIH to take a more coordinated approach to the development and funding of trans-agency initiatives by asking each IC to pool a very small proportion of their appropriation in a Common Fund for shared needs. This is true not only because of the difficult budgets, but also because many of the most exciting scientific opportunities and pressing public health challenges we now face cut across the mission areas of multiple institutes and centers. Thus, the creation of this new trans-NIH funding stream will actually enable the NIH to be more proactive in addressing emerging scientific needs and opportunities; to fund high-risk, high-impact science; and to incubate and launch pilot efforts that have transforming potential for all of science.

THE HEART TRUTH ROAD SHOW

Question. As a member of the Congressional Heart and Stroke Coalition, I am concerned that heart disease remains the leading cause of death of women in the United States, but many women do not realize this fact. I know that for the past several years, the NIH has been working with the fashion industry in your Heart Truth Campaign to increase women's knowledge about their No. 1 killer and that the Heart Truth Road Show stopped in Pittsburgh recently. Please explain to the Committee about the progress of this initiative?

Answer. The National Heart, Lung, and Blood Institute's (NHLBI) The Heart Truth campaign continues to flourish, extending the reach of the campaign in a variety of ways.

- As the campaign ambassador, First Lady Laura Bush is leading the federal effort to give women a personal and urgent wake-up call about their risk of heart disease, participating in more than a dozen Heart Truth events around the nation over the past 3 years.
- Corporate partners, including General Mills, Minute Maid, and DermaDoctor, have featured the campaign's Red Dress (emblematic of the message "Heart disease doesn't care what you wear; it's the killer of women") on more than 60 million product packages. Johnson & Johnson, L'eggs hosiery, Benecol, Starkist Tuna, and Celestial Seasonings have promoted The Heart Truth campaign and Red Dress logo in newspaper advertising inserts, resulting in a combined circulation of 370 million.
- The Red Dress Collection 2006 Fashion Show took place on the third annual National Wear Red Day—Friday, February 3, 2006. People throughout the country participated in the day's celebration to increase awareness of women's heart disease.
- The Heart Truth Road Show visited shopping malls in Pittsburgh, Memphis, and Washington, DC, in the spring of 2006 to raise awareness about women and heart disease by helping participants learn about risk factors; providing free health screenings including blood pressure, body mass index, total blood cholesterol, and blood glucose; and disseminating educational materials.
- The campaign launched "Know The Heart Truth" in April 2006, an initiative that is recruiting and training health advocates and educators in local communities to increase awareness about women and heart disease. The Heart Truth has also formed partnerships with leading organizations representing women of color to engage in national and local activities, including a faith-based initiative, to help women reduce their risk for heart disease.

The impact of The Heart Truth campaign is already becoming apparent. Awareness of heart disease as the leading cause of death among American women in-

creased from 34 percent in 2000 to 46 percent in 2003 to 55 percent in 2005. A 2005 survey commissioned by WomenHeart found that 60 percent of U.S. women agreed that the Red Dress makes them want to learn more about heart disease. Twenty-five percent of women recalled the Red Dress as the national symbol for women and heart disease awareness and 45 percent agreed that it would prompt them to talk to their doctor and/or get a check-up. A Lifetime Television Women's Pulse Poll released in February 2006 showed that women are increasingly aware of the dangers of heart disease. Thirty-nine percent of survey participants recognized the Red Dress as the national symbol for women and heart disease awareness, up from 25 percent in 2005.

STROKE

Question. Following up on language from last year's congressional report, please provide this Committee with highlights of implementation progress on the Stroke Progress Review Group report.

Answer. In 2001, the NINDS convened the first meeting of the Stroke Progress Review Group (SPRG) to identify and prioritize scientific opportunities and needs in stroke research. One hundred forty prominent scientists, clinicians, patient advocates, and industry representatives participated and developed a set of scientific and resource recommendations that the NINDS assembled in a Report of the SPRG in 2002. In 2003, the chairs of the SPRG meeting reprioritized their recommendations and identified a subset of high priorities for stroke research in an Implementation Report. Many of the following research activities address the scientific research and resource priorities identified by the SPRG in its 2002 Report and 2004 Implementation Report.

The NINDS is funding a wide range of studies on the basic biology of stroke, including the role of the blood-brain barrier (BBB; the cellular barrier that controls the exchange of substances between the blood and the nervous system) and the neurovascular unit (NVU; the functional "unit" comprised by brain blood vessels, glial support cells, and neurons). Understanding the function of the NVU and the BBB in stroke is critical to developing strategies for treating and preventing stroke and related conditions such as vascular cognitive impairment (VCI). NINDS is supporting a variety of stroke-related studies focused on the roles of the NVU and the BBB under two recent Program Announcements with set-aside funding. To more fully understand the biological basis of VCI, the Institute held a workshop in June 2006 to discuss the cell biology of VCI and develop recommendations to accelerate research in this area.

To facilitate the translation of basic research findings into the clinical setting, NINDS is planning to expand its Specialized Programs of Translational Research in Acute Stroke to include seven programs across the country participating in clinical trials, training of research fellows, and translational research on stroke. In addition, NINDS released two new grant solicitations to address barriers to translational research in stroke.

The NINDS also continues to fund many clinical trials involving potential interventions and preventive strategies for stroke. To improve outcomes for stroke patients in emergency-room settings, the NINDS is developing a Neurological Emergencies Treatment Trials (NETT) Network of emergency medicine physicians, neurologists, and neurosurgeons, and plans to fund the clinical coordinating center component of the NETT in fiscal year 2006. The Institute is also supporting research on the causes of stroke among high risk groups, improved methods for diagnosing stroke, and a range of educational outreach programs to increase awareness of stroke risk factors and symptoms.

In September 2006, the NINDS will sponsor another meeting of the SPRG to assess research progress in stroke, evaluate current priorities, and identify new opportunities for advancing stroke research. Prior to the meeting, 16 working groups will assess progress and develop recommendations for future priorities on topics ranging from genetics of stroke to recovery and rehabilitation. NINDS solicited information from the stroke research community on research progress and remaining needs and research gaps, and will provide this feedback to the SPRG participants prior to their deliberations. Following the September meeting, the SPRG will produce a mid-course implementation report that reflects the current status of stroke research and identifies new priorities.

CLINICAL AND TRANSLATIONAL SCIENCE AWARDS

Question. You have announced that by the year 2010, the GCRC program will have been phased out and the funding transferred to a new program. How are you going to assure that the CTSA's maintain or enhance services currently provided by

the GCRCs including specialty nursing care, patient facilities, laboratory testing, and specialized monitoring and diagnostic capabilities?

Answer. Applicants for the Clinical and Translational Science Awards (CTSAs) are asked to propose a center, department, or institute for clinical research that will transform the clinical and translational research environment at their institution. Up to \$6 million additional funds may be requested in addition to certain National Center for Research Resources (NCRR) and NIH Roadmap awards held by the institution at the time of application. These additional funds may be used to transform the local, regional, and national environment for clinical and translational science, thereby increasing the efficiency and speed of clinical and translational research. By introducing CTSAs as an increase in support, NIH is allowing applicants to retain such services as are currently provided by the General Clinical Research Centers (GCRCs) that they deem needed for their clinical research, such as inpatient and outpatient facilities, laboratory testing, and specialized monitoring and diagnostic capabilities.

Question. You have announced that by the year 2010, the GCRC program will have been phased out and the funding transferred to a new program. How will you monitor the impact on the vitally important clinical research support currently provided to patients and investigators through the GCRCs?

Answer. NIH staff review GCRC Annual Reports, communicate frequently with grantees, and attend annual meetings with Center grantees in Washington, DC. Clinical and Translational Science Awards likewise will submit Annual Reports and will establish Steering Committees on which NIH will be represented. These various tools and forums provide opportunities to assess the impact of the Clinical and Translational Science Awards and General Clinical Research Centers and will assure NIH of the requisite monitoring for impact on clinical research support.

Question. You have announced that by the year 2010, the GCRC program will have been phased out and the funding transferred to a new program. Will institutions that lose their existing GCRC funding and do not receive CTSA awards be able to support patient-oriented research facilities and services?

Answer. The 60 CTSAs that NIH plans to award could support over 90 percent of the institutions that currently have GCRCs. Researchers that perform patient oriented research at institutions that do not receive CTSAs may apply for investigator-initiated NIH research supported by a variety of NIH grant mechanisms including Research Project and Research Program Projects and Centers grants. Additional sources of research support for investigators may come from Research Foundations, partnerships with industrial sponsors and institutional funds.

Question. You have announced that by the year 2010, the GCRC program will have been phased out and the funding transferred to a new program. Will researchers in these institutions have to cancel planned patient-oriented research projects because of inadequate facilities? Certainly, the NIH budget is too constrained to provide this support through other competitive mechanisms.

Answer. Researchers in the institutions that do not receive Clinical and Translational Science Awards may apply for investigator initiated NIH research supported by numerous NIH grant mechanisms including Research Project and Research Program Projects and Centers grants. Research Foundations, partnerships with industrial sponsors, and institutional funds may also provide additional sources of research support for investigators.

Question. The K12 training mechanism is required for the CTSA award. Why isn't the GCRC M01 mechanism required? The RFA appears to marginalize the GCRCs and their functions, and I am concerned about that. Why not require the M01 mechanism in the CTSA award RFA in 2007?

Answer. Applicants for a CTSA are required to include a Mentored Clinical Research Scholar Award (K12) component in their proposal so as to promote clinical and translational research as a distinct discipline. There is no requirement for applicants to be K12 awardees for them to apply for a CTSA. NCRR has not made an M01 award an eligibility requirement for a CTSA application in the expectation that certain new affiliations amongst institutions that do not currently hold an M01 award would be strong enough to compete successfully. CTSAs will support the discipline of clinical and translational science and the needs of its researchers, so applicants are encouraged to look beyond the constraints of M01 awards and to propose novel concepts, methodologies, and approaches that could be integrated into a comprehensive, effective, and efficient researcher-, trainee-, and participant-centered clinical research program.

Question. Could NIH maintain a GCRC or mini-GCRC program for institutions that have had strong GCRCs, historically, but do not receive CTSA awards.

Answer. NCRR has received wide support for the new CTSA program, so we believe that the purposes of clinical research will best be served by a smooth and unin-

interrupted transition. Several new consortia are expected to apply for CTSA and clinical research at those sites that compete well in the peer review process should not be delayed by prolongation of the GCRC program. Retaining the GCRC program would limit the funding available for the CTSA program and NIH believes that this would be detrimental to the needs and interests of the majority of clinical investigators.

Question. Have you considered the possibility of a “pause” after the second year of implementation to evaluate the effectiveness and impact of the new CTSA program before proceeding with additional awards?

Answer. The combination of Annual Reports with Clinical and Translational Science Award Steering Committees will assure NIH of the requisite evaluation opportunities during their implementation. In the event that changes are required to optimize the award functionality, they can be made without the delays that would be incurred through a “pause” in making awards.

Question. Do you have a fall-back plan if the budget is not sufficient to accommodate the implementation of the CTSA program as you envision it?

Answer. Transformation of Clinical Research infrastructure programs from GCRCs to CTSAAs will be funded principally by NCRR appropriated funds, with additional funds from the NIH Roadmap for Medical Research. The project period for CTSA grants is 5 years, and NIH is planning for an additional 5-year competitive renewal of these awards. The fiscal year 2006 funding level for the combined CTSA/GCRC program is \$322,740,000 and their estimated fiscal year 2007 funding level is \$361,200,000. NIH plans to award four to seven CTSAAs in fiscal year 2006, to increase the number of awards annually, and to have 60 CTSAAs in place by 2012. While changes in Congressional Appropriations would affect both the GCRC and CTSA programs in parallel, the transformation of the GCRC program to CTSAAs is occurring in response to user demand.

POLYCYSTIC KIDNEY DISEASE

Question. The Food and Drug Administration has granted “Fast Track” designation for Tolvaptan, a promising drug therapy designed to retard disease progression in polycystic kidney disease (PKD) and thus prevent kidney failure. What does the NIH plan to do to make the most of this discovery and foster the development of further PKD therapies?

Answer. The NIH is committed to research that will pursue opportunities to combat polycystic kidney disease (PKD)—a serious, burdensome, and costly disease. Within the NIH, the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) supports a diverse portfolio of basic and clinical research into the underlying biology of and possible therapies for PKD. The Interdisciplinary Centers for Polycystic Kidney Disease Research are important components of this research portfolio. The NIDDK recently renewed funding for four Centers for five additional years. Three of the Centers focus on the more common autosomal dominant PKD (ADPKD), and will explore extensively the basic and clinical functional changes seen in ADPKD. The fourth is a Research and Translational Core that focuses on autosomal recessive PKD (ARPKD) and will make available to investigators in the field a broad range of model research systems and reagents for the study of ARPKD.

The Institute also has two other major research projects related to PKD—the HALT-PKD trial network, and the Consortium for Radiologic Imaging Studies of PKD (CRISP) cohort study. CRISP was established to develop innovative and standardized imaging techniques and analyses that would allow clinicians to reliably follow disease progression of ADPKD. This four-year study followed 240 PKD patients with annual glomerular filtration rate evaluation (a measure of kidney function), and magnetic resonance imaging to assess changes in kidney volume over time. The first phase of CRISP was recently completed, and the primary study results were published in the *New England Journal of Medicine* in May 2006 (NEJM 354: 2122–2130, 2006). Although the preliminary findings show promise for use of imaging methods and structural endpoints for tracking progression of ADPKD, the NIDDK has extended the CRISP cohort study for another five years, in order to collect additional structure and function data on enrolled subjects. Additional data from CRISP II will enable investigators to assess how reliably structural changes can predict functional kidney changes over time in ADPKD. The CRISP II investigators are currently developing the protocol for the next phase of the study.

The Polycystic Kidney Disease Clinical Trials Network, co-funded by the PKD Foundation, is conducting two phase III-type studies in the HALT-PKD trial—one in patients with early kidney disease and another in patients with more advanced disease. HALT-PKD is testing whether blockade of the renin-aldosterone-angiotensin system, with angiotensin-converting enzyme inhibitor monotherapy or

combination angiotensin-converting enzyme inhibitor and angiotensin receptor blocker, will slow the progression of ADPKD. A partnership was also negotiated with industry to provide medications for testing in these studies. The HALT-PKD trial in subjects with early kidney disease is novel in that it is implementing the CRISP imaging methods in order to determine how reliable the methods are for interventional studies in ADPKD. The ability to reliably implement imaging methods for trials of ADPKD will have a significant impact on planning future interventional studies of new therapeutics in this disease. The HALT-PKD studies began enrolling patients in January 2006, and will be the largest interventional trial ever conducted in ADPKD.

NATIONAL PRIMATE RESEARCH CENTER

Question. The fiscal year 2006 Labor-HHS-Education Appropriations bill provided the NIH Office of AIDS Research with up to \$4 million to spend for construction or renovation necessary to expand a breeding colony for non-human primates for AIDS research, which is intended to be collaborative effort amongst the National Primate Research Centers. What progress has been made on that effort, and what is the expected completion date?

Answer. Although the fiscal year 2006 bill allows the Office of AIDS Research (OAR) to utilize funds for construction for the national breeding resource facility, funds will not be used for that purpose in fiscal year 2006. In late fiscal year 2005, the Tulane National Primate Research Center successfully competed for the first phase of a national breeding resource facility project. However, construction capability in this region has been limited in the aftermath of Hurricane Katrina. Thus the second phase of this project has not proceeded as scheduled. Consequently, OAR cannot use this provision of the fiscal year 2006 appropriations bill this year. Instead, OAR provided funds to NCRR to support AIDS-related research infrastructure needs and increased operating expenses, such as unanticipated high energy costs, at the National Primate Research Centers (NPRCs). A timeline for completing the national breeding resource facility project is being reassessed.

QUESTIONS SUBMITTED BY SENATOR TOM HARKIN

COLLABORATION AMONG INSTITUTES

Question. Dr. Zerhouni, one of the most common complaints I hear from advocacy groups is that they can't get multiple NIH institutes and centers (ICs) to work together on common goals. Consider diseases like scleroderma, neurofibromatosis or epilepsy, all of which fall under the jurisdictions of more than one IC. In each case, one IC might be designated as taking the lead on the disease, but other ICs also share the responsibility for conducting research on it. Too often, unfortunately, patients complain that the ICs don't collaborate. Sometimes the patients themselves practically have to drag a researcher from one institute into a meeting with a researcher from another institute, just to get them to talk.

I know you're well aware of this problem. It's an issue that the National Academies addressed in its report on NIH's structure in 2003. What are you doing to improve the situation?

Answer. In 2002, I began a process called the Roadmap for Medical Research that was designed to identify major opportunities and gaps in biomedical research that no single institute at NIH could tackle alone to make the biggest impact on the progress of medical research. A primary accomplishment of the Roadmap was internal "functional integration" of the 27 institutes and centers (IC) to plan, implement and fund initiatives that go beyond the mission of any one IC. These accomplishments led to creation of the Office of Portfolio Analysis and Strategic Initiatives (OPASI) which has begun to institutionalize these processes. The establishment of OPASI represents a major organizational change at NIH aimed primarily at addressing challenges in the coordination of biomedical research of benefit to every IC. Using a combination of approaches such as agency-encompassing portfolio analysis and establishment of a common fund for shared needs, OPASI will synergize diverse components of the NIH toward the attainment of common goals more efficiently. Continuing the tradition of the NIH Roadmap, this office will also support well-developed initiatives that address areas of science which do not clearly fall within the mission of any one IC or program office. This makes OPASI a natural space for NIH ICs to work together on broad-reaching opportunities which will impact multiple aspects of public health and disease intervention.

CONFLICTS OF INTEREST

Question. Last August, NIH announced the final ethics rules on conflicts of interest. What impact are they having on employee retention and recruitment, and on interactions between NIH scientists and outside associations, such as trade groups and scientific associations?

Answer. Regarding Employee retention and recruitment. In the preamble to the final rule (published in August 2005), we stated that we would review the rule to “evaluate continued adequacy and effectiveness in relation to current agency responsibilities.” We are particularly interested in learning about any effects that the prohibited holding and outside activities provisions of the rule have had on hiring and retention. We are currently in the process of conducting a survey of current NIH employees, collecting their feedback related to the new regulations. In separate surveys in the coming months, we intend to ask former employees (those who left the NIH after January 1, 2005) and potential employees their opinions as well.

Interactions between NIH scientists and outside associations, such as trade groups and scientific associations. The regulations do not affect official duty interactions that scientists may have with trade groups or scientific associations.

PANDEMIC FLU

Question. We are all concerned about how long it would take between the time that we detected a pandemic flu virus in the United States and when we could create a vaccine for it. Right now, if a pandemic were to occur, I understand that it would take almost six months to produce a vaccine, using our current egg-based methods.

HHS recently invested \$1 billion in the development of new cell-based technologies to produce a pandemic vaccine. We’re all looking forward to the results. But even if successful, a cell-based vaccine would not be immediately available at the time of a pandemic.

The current methods of vaccine development are commonly referred to as the “one drug, one bug” philosophy—develop a vaccine for each flu strain or strains. But that means that you have to identify the “bug” or flu strain before you can begin to manufacture a vaccine. However, I have heard that there is work being done to develop a vaccine that would address all strains of the flu—a “one drug, many bugs” plan. Is NIH supporting this type of research? Does it have promise?

Answer. The National Institute of Allergy and Infectious Diseases (NIAID) is supporting research and development of alternate approaches to dealing with the threat of emerging and re-emerging infectious diseases such as influenza.

For example, NIAID is pursuing the development of a “universal vaccine” that protects against multiple virus strains such as those resulting from antigenic drift associated with seasonal influenza and antigenic shift associated with pandemic influenza. As influenza viruses circulate, the genes that determine the structure of their surface proteins undergo small changes. Sometimes the change in the genes results in a slight change in the antigenic properties of the protein, a process commonly referred to as “antigenic drift.” Antigenic drift is the basis for the changes in seasonal influenza observed during most years, and is the reason that we must update influenza vaccines annually. Influenza viruses also can change more dramatically. For example, viruses sometimes emerge that can jump species from natural reservoirs, such as wild ducks, to infect domestic poultry, farm animals, or humans. When an influenza virus jumps species from an animal, such as a chicken, to infect a human, the result is usually a “dead-end” infection that cannot readily spread further in the human population. However, mutations in the virus could develop that allow human-to-human transmission. Furthermore, if an avian influenza virus and another human influenza virus were to simultaneously co-infect a person or animal, the two viruses might swap genes, possibly resulting in a virus that is readily transmissible between humans, and against which the population would have no natural immunity. These types of significant changes in influenza viruses are referred to as “antigenic shift.” When an “antigenic shift” occurs, a global influenza pandemic can result. Historically, pandemic influenza is a proven threat. In the 20th century, influenza pandemics occurred in 1918, 1957, and 1968.

The NIAID is supporting a number of research projects to develop a vaccine that induces a potent immune response to the common elements of the influenza virus that undergo very few changes from season to season and from strain to strain. Although this is a difficult task, such a “universal” influenza vaccine would not only provide continued protection over multiple seasons, it might also offer protection against a newly emerged pandemic influenza virus and thus substantially reduce the susceptibility of the population to infection by any influenza virus—making the

country far less vulnerable to influenza viruses emerging from avian and other animal sources.

One relatively stable element of the influenza virus is a protein called M2. The external portion of the M2 protein is very similar in influenza viruses from year to year and from strain to strain. A “universal” influenza vaccine targeting the M2 protein, or other conserved elements, could be protective against a range of influenza strains. NIAID-supported researchers have demonstrated that vaccines made with bioengineered versions of M2 can protect mice from lethal influenza virus. The scientists now are testing cross-reactivity between different species and strains of influenza, examining how long the immunity provided by these vaccines lasts, and evaluating whether the influenza viruses can evade these vaccines by developing mutations in their M2 proteins.

In addition, researchers at the NIAID Vaccine Research Center (VRC) are developing and testing gene-based influenza vaccines that will protect against multiple strains of influenza. As a first step, initial candidate vaccines, each containing the gene encoding the hemagglutinin (H) surface protein of an influenza virus isolated from a recent human outbreak of influenza (H1N1, H3N2 or H5N1), have already shown promise in animal studies. VRC researchers plan to develop additional gene-based vaccines for all common variants of hemagglutinin, as well as other influenza viral proteins, such as nucleoprotein and the M2 protein. In the future, the VRC will incorporate both conserved and variable genes from multiple influenza strains into DNA and adenovirus vectors that can readily be produced by existing manufacturing processes.

A second approach, while not technically a vaccine, is an immune enhancer which specifically targets a component of the immune system and enhances one’s ability to respond to a broad range of microbial threats. Studies of the human innate immune system, which is comprised of “first responder” cells and other defenses that provide a first line of defense against a wide variety of pathogens, have been moving forward rapidly. These advances suggest it may be possible to develop a relatively small set of fast-acting, broad-spectrum countermeasures that can boost innate immune responses to many pathogens or toxins, including influenza. The capability to boost the innate immune system also could lead to the development of more powerful vaccine additives, called adjuvants, that can increase vaccine potency. The concept of immune enhancers has been demonstrated in early stage clinical studies, but requires further research and development to be applied to pandemic influenza vaccination.

QUESTIONS SUBMITTED BY SENATOR DANIEL K. INOUE

TRADITIONAL HEALING PRACTICES

Question. Last year, at my request, Dr. Donald Lindberg, Director of the National Library of Medicine, visited one of our Native Hawaiian Healing programs at Papa Ola Lokahi for the purpose of conducting “listening circles” to discuss the needs for preservation and documentation of traditional cultural healing practices. I am very interested in a report of his findings from this visit. I am most appreciative of the National Library of Medicine’s continued interest and support of Native Hawaiian issues.

Answer. Early this year NLM convened a working group to examine both the feasibility of an exhibition on Native health and healing, and NLM’s role in collecting and preserving information about traditional medicine. As a result of this working group, NLM has reviewed its collection to develop policies, as well as examined its collection in these areas. Subsequently, the Library has made an effort to collect modern publications such as all the items in the Bishop Museum’s (Honolulu, HI) current catalog as well as their out of print materials.

In addition to purchasing standard published materials, NLM is also obtaining input from Native American (including Native Hawaiian) healers, leaders, educators, and others, on appropriate collection and preservation policies. Over the past year, since the series of Listening Circles the NLM participated in with different Native Peoples, NLM staff have met with many such individuals to gain insight into the issues of collecting and preserving information about traditional healing practices. For example, in February, NLM staff met with librarians and curators from the Bishop Museum, Hawaiian Historical Society, The Hawaiian Mission Children’s Society Library, and the University of Hawaii to gather information to planning a larger follow-up meeting.

This meeting, to include NLM staff, occurred in July 2006, and a report of findings from this visit will be prepared.

DEVELOPING NURSE RESEARCHERS

Question. A long-standing supporter of the National Institute for Nursing Research, I am pleased with the extensive array of research initiatives that have been undertaken by the Institute. I am particularly pleased with those endeavors that are directed at developing the pool of nurse researchers who also become nurse faculty. Another important initiative is training support for fast-track baccalaureate to doctoral program participants. I welcome news of the Institute's progress in facilitating research projects in rural areas that serve minority students via community colleges.

Answer. NINR considers the development of nurse researchers and nurse faculty to be a fundamental component of its research mission. Indeed, developing nurse investigators will be an overarching goal in the Institute's new strategic plan for 2006–2010.

Approximately 7 percent of NINR's budget supports the Institute's Centers programs, which are used to develop the nursing research infrastructure and train new investigators. In addition to our ten Core and nine Exploratory Centers, we have co-sponsored a joint initiative with the National Center on Minority Health and Health Disparities that supports partnerships between established, research-intensive institutions and growing, minority-serving institutions. These Nursing Partnership Centers on Reducing Health Disparities, involving 17 schools of nursing, will increase health disparities research and broaden the diversity of the nurse scientist pool. Several of these Centers are located in rural areas or serve rural and other underserved populations. These Centers represent a major investment aimed at expanding the cadre of nurse scientists involved in health disparities research.

BACCALAUREATE TO DOCTORAL PROGRAMS

Question. A long-standing supporter of the National Institute for Nursing Research, I am pleased that the Administration has continued funding of this program. However, what impact will the \$1 million reduction have on the National Institute of Nursing Research's development of initiative that supports fast-track baccalaureate-to-doctoral programs? These programs were proposed to help increase the number of nursing faculty and in turn decrease the number of qualified nursing school candidates who were turned away in prior years.

Answer. The overall reduction of \$792,000 in the fiscal year 2007 budget request of \$136.6 million for the National Institute of Nursing Research (NINR) will have no impact on its programs that fast-track baccalaureate-to-doctoral nurses to increase the number of nursing investigators. These programs are supported within the Research Training mechanism in NINR, and the fiscal year 2007 President's Budget maintains the current level of support of this activity. NINR remains committed to developing the next generation of nurse scientists. NINR encourages and supports strategies to change the career trajectory of nurse scientists. The Institute emphasizes early entry into research careers, including fast-track baccalaureate-to-doctoral programs, and supports pre-doctoral and postdoctoral nurses who are the future researchers and nursing faculty.

CANCER CENTERS

Question. The National Cancer Institute has had great success and demonstrated value in its system of cancer centers across the country. When awarding core grants for cancer research, is attention paid to geographic and ethnic diversity to ensure that results will capture the often significant differences in outcomes among various ethnic groups and lifestyles?

Answer. The NCI-designated Cancer Centers are vital parts of a national strategy to reduce the suffering and death due to cancer. The NCI Cancer Centers Program provides critical infrastructure for academic and research institutions throughout the United States that provide broad based, coordinated, interdisciplinary programs in cancer research. These institutions are characterized by scientific excellence and a capacity to integrate various research approaches focused on the problem of cancer. Generally, in order to become an NCI-designated Cancer Center, an institution must have a large cancer-relevant grant funding base; substantial institutional commitment in the form of space, resources, and authorities provided to the Center Director; a synergistic organization of transdisciplinary research across all scientific areas of the institution; and, specifically for comprehensive centers, community outreach, education, and training activities.

While the NCI designation is based solely on an evaluation of the science, Centers deliver medical advances to patients and their families; provide state-of-the-art care and access to clinical trials; serve as the major training ground for new clinicians

and researchers; and have the strong links with national, state, and local agencies and advocacy groups needed to address cancer issues most relevant to their communities.

Examples of strategies focused on the geographic reach of Cancer Center services include:

- Minority Institution/Cancer Center Partnership Programs (MI/CCP).*—The MI/CCP, which partner Minority-Serving Institutions (MSIs) with existing NCI-designated Cancer Centers, was established in 2000 to take maximum advantage of their respective expertise and experience. The program is designed to foster development of independent cancer research programs and minority career scientists in MSIs and to improve minority-focused outreach and training efforts in NCI-designated Cancer Centers. Participation in this program better positions MSIs to compete for independent NCI designation and/or to form equal and permanent research alliances with existing NCI-designated Cancer Centers. These partnerships are expected to enable the NCI-designated Cancer Centers to realize substantial progress in their efforts to implement effective research, outreach, and education programs that truly benefit minority populations.
- Affiliations and Consortia.*—Realizing that many institutions serving minorities may not have the research capability or the desire to apply for NCI designation independently, NCI revised the Cancer Center guidelines to encourage the development of affiliations and consortia. We specifically encourage consideration of partnerships that address cancer in minority and other underserved populations.
- Emphasized Integration.*—Through NCI's "Discovery, Development, Delivery" continuum, we expect the continued development of links between existing Cancer Centers, their affiliates and partners in research; as well as state, municipal, and community-based private organizations. NCI is actively seeking mechanisms to foster both vertical integration (i.e., from the Cancer Centers through the community layers they serve) and horizontal integration (i.e., across Cancer Centers and a nationwide network of public and private partners) of the benefits of cancer research. This integration provides a more unified approach to reducing cancer and cancer risk, and more uniform delivery of the benefits of cancer research into all communities.

NCI recognizes that the Cancer Research Center of Hawaii is unique in the community it serves. NCI program staff regularly consults with existing NCI-designated centers on approaches for enhancing representation of underserved populations, and provides support and direction to Center and institutional leadership on how to maintain NCI designation; the latter activities are viewed as particularly critical for Centers with significant minority and other underserved populations.

NCI continues to pay close attention to the Cancer Centers geographic placement. The latest planning grants for NCI Cancer Research Centers (an initial step to gaining designation) have gone to areas without an NCI-designated Center (University of Louisville, University of Oklahoma, Emory University, Medical University of South Carolina, and Howard University). The University of New Mexico, a former planning grant recipient, received Cancer Center designation last year. NCI also continues to advise emerging centers in a number of other underrepresented areas around the country on an informal basis.

Additionally, the Cancer Centers themselves are increasingly establishing their own networks with community hospitals and private oncology practices and extending the benefits of care and clinical trials further into communities not previously reached.

CONSULTATION PROTOCOL

Question. I am pleased that the National Library of Medicine and the National Cancer Institute have made substantial efforts to incorporate, within their program areas, resources to address Native Hawaiian health issues and concerns. The Secretary's latest directive on consultation directs the Intra-Department Council on Native American Affairs to incorporate Native Hawaiian health needs and concerns within the consultation framework for agencies within the Department of Health and Human Services similar to that afforded American Indians and Alaska Natives.

Would the National Institutes of Health be willing to engage in discussions with Papa Ola Lokahi (Native Hawaiian Health Board) on how best the lessons learned working with the National Library of Medicine and the National Cancer Institute can be incorporated within all the Institutes of the National Institutes of Health to develop an agency-wide consultation protocol for the National Institutes of Health and Native Hawaiians similar to that afforded to American Indians and Alaska Natives?

Answer. The NCMHD has established a trans-NIH Committee to work on the NIH implementation of the Department of Health and Human Services' tribal consultation policy. As the committee prepares the NIH-wide tribal consultation protocol, it will look at various best practice models among the Institutes and Centers, including the National Library of Medicine and National Cancer Institute's models for lessons learned that could be incorporated into the protocol and be beneficial to Papa Ola Lokahi and other Native Hawaiians. The NIH recognizes the importance of listening, dialoguing, and developing relationships prior to developing programs and services, and would be willing to hear the suggestions of Papa Ola Lokahi.

QUESTIONS SUBMITTED BY SENATOR HARRY REID

CHRONIC FATIGUE SYNDROME (CFS)

Question. How many Chronic Fatigue Syndrome (CFS) specific grant applications were received, reviewed and funded for fiscal year 2004 and fiscal year 2005?

Answer. In fiscal year 2004, 17 CFS-specific grant applications (R01) were received and reviewed; 2 were awarded. One P50, a specialized center, was received and awarded. One R13, a conference grant, was received and awarded. In fiscal year 2005, eight CFS-specific grant applications (R01) were received and reviewed; one was awarded. One K12, Physician Scientist Award, was received but not awarded.

Question. Please provide a detailed list of the studies, institutions, lead researchers and individual grant amounts for all CFS studies funded in fiscal year 2004 and fiscal year 2005.

Answer. The information requested is included in the following tables compiled by the OD Budget Office.

NATIONAL INSTITUTES FOR HEALTH—FUNDING FOR CHRONIC FATIGUE SYNDROME FISCAL YEAR 2004

[Whole dollars]

IC	Project number	Principal investigator	Institution	State	Project title	Amount
NHLBI	5 R01 HL045462	COLLINS, TUCKER O	CHILDREN'S HOSPITAL (BOSTON)	MA	TRANSCRIPTIONAL REGULATION OF E-SELECTIN	\$177,750
NHLBI	5 R01 HL054926	ISCHIROPOUL OS, HARRY	CHILDREN'S HOSPITAL OF PHILA-DELPHIA	PA	REACTIVE SPECIES IN VASCULAR DISEASE-INIURY	170,000
NHLBI	5 R01 HL055591	LOWASNEY, JON W	NORTHWESTERN UNIVERSITY	IL	MOLECULAR BASIS FOR PROTEIN-PHOSPHOLIPID INTER-ACTION	148,500
NHLBI	5 R01 HL056850	CLEMMONS, DAVID R	UNIVERSITY OF NORTH CAROLINA CHAPEL HILL	NC	MECHANISMS BY WHICH IGF-I STIMULATES SMOOTH MUS-CLE CELLS	203,694
NHLBI	5 R01 HL059459	FREEMAN, ROY	BETH ISRAEL DEACONESS MEDICAL CENTER	MA	ORTHOSTATIC INTOLERANCE IN CFS	392,186
NHLBI	2 R01 HL061388	CRANDALL, CRAIG G	UNIVERSITY OF TEXAS SW MED CTR/DALLAS	TX	HEAT STRESS AND CIRCULATORY CONTROL	61,066
NHLBI	5 R01 HL066007	STEWART, JULIAN M	NEW YORK MEDICAL COLLEGE	NY	CIRCULATORY DYSFUNCTION IN CHRONIC FATIGUE SYN-DROME	252,000
NHLBI	5 R01 HL067422	CRANDALL, CRAIG G	UNIVERSITY OF TEXAS SW MED CTR/DALLAS	TX	SKIN COOLING TO IMPROVE ORTHOSTATIC TOLERANCE	131,500
NHLBI	5 R01 HL070215	CALDWELL, ROBERT W	MEDICAL COLLEGE OF GEORGIA	GA	ENDOTHELIAL CELL DYSFUNCTION IN OXIDATIVE STRESS MODELS	125,562
TOTAL, NHLBI						1,662,258
NINDS	1R13NS047105-01	HORTOBAGYI, TIBOR	EAST CAROLINA UNIVERSITY	SC	INTERNATIONAL SYMPOSIUM ON MOTOR CONTROL USING TMS	2,250
NINDS	5Z01NS002979-06	GOLDSTEIN, DAVID	NINDS	MD	CLINICAL NEUROCARDIOLOGY: CATECHOLAMINE SYSTEMS IN STRESS AND DISEASE	531,506
TOTAL, NINDS						533,756
NIAID	1 R01 AI05601401A1	SULLIVAN, PATRICK F	UNIVERSITY OF NORTH CAROLINA CHAPEL HILL	NC	MICROARRAYS & PROTEOMICS IN MZ TWINS DISCORDANT FOR CFS	255,301
NIAID	5 R01 AI042403-07	BARANIUK, JAMES N	GEORGETOWN UNIVERSITY	DC	MECHANISMS OF RHINITIS IN CFS	232,800
NIAID	5 R01 AI049720-05	JASON, LEONARD	DE PAUL UNIVERSITY	IL	ACTIVITY INTERVENTION FOR CHRONIC FATIGUE SYN-DROME	266,169
NIAID	5 R01 AI051270-03	TAM, PATRICIA E	UNIVERSITY OF MINNESOTA TWIN CITIES	MN	VIRAL DSRNA AS A MEDIATOR OF CHRONIC MUSCLE DIS-EASES	334,125

NIAD	2 R01 A054478-02	NATLSON, BENJAMIN H	UNIV OF MED/DENT NJ NEWARK	NU	SLEEP AND CYTOKINES IN CHRONIC FATIGUE SYNDROME	334,904
TOTAL NIAD	1,423,299
NICHD	R01HD043301-02	TAYLOR, RENE E R	UNIVERSITY OF ILLINOIS AT CHICAGO	IL	CHRONIC FATIGUE SYNDROME IN ADOLESCENTS	267,009
TOTAL NICHD	267,009
NIAMS	5-R01-AR-47678-03	BUCHWALD, DEBRA S	UNIVERSITY OF WASHINGTON	WA ...	ARE FIBROMYALGIA AND CHIARI I MALFORMATION RELATED?	146,712
TOTAL NIAMS	146,712
NIMH	5K23MH001961-04	FRIEDBERG, FRED	STATE UNIVERSITY NEW YORK STONY BROOK	NY ...	PSYCHIATRIC COMORBIDITY IN CHRONIC FATIGUE SYNDROME	148,923
TOTAL NIMH	148,923
NINR	R01-A049720-05	LEONARD, JASON	DE PAUL UNIVERSITY	IL	ACTIVITY INTERVENTION FOR CHRONIC FATIGUE SYNDROME	100,000
TOTAL NINR	100,000
NCRR	2M01RR000037-44	SMITH, MARK	UNIVERSITY OF WASHINGTON	WA ...	THE EFFECT OF PARENTAL CHRONIC FATIGUE SYNDROME ON OFFSPRING	29,494
NCRR	3P41RR002305-20S1 ..	MCCULLY, KEVIN	UNIVERSITY OF PENNSYLVANIA	PA ...	CHRONIC FATIGUE SYNDROME	5,742
NCRR	5M01RR000039-44	PAPANICOLA OIU, DIMITRIS A	EMORY UNIVERSITY	GA ...	EFFECTS OF CORTICOTROPIN-RELEASING HORMONE INFUSION IN NORMAL FEMALES	179,251
NCRR	5M01RR000042-44	WILLIAMS, DAVID A	UNIVERSITY OF MICHIGAN AT ANN ARBOR	MI ...	SUBJECT REGISTRY: INTERDISCIPLINARY STUDIES OF CHRONIC MULTI-SYMPTOM ILLNESSES	9,149
NCRR	5M01RR000046-44	LIGHT, KATHLEEN C	UNIVERSITY OF NORTH CAROLINA CHAPEL HILL	NC ...	FACTORS IN ARTHRITIS, CFS, FIBROMYALGIA & TEMPOROMANDIBULAR DISORDERS	74,144
NCRR	5M01RR000052-43	ROWE, PETER C	JOHNS HOPKINS UNIVERSITY	MD ..	DISORDERED RESPONSES TO ORTHOSTATIC STRESS IN . . . GULF WAR SYNDROME SYMPTOMS	7,991
NCRR	5M01RR000052-43	SCHWARTZ, CINDY	JOHNS HOPKINS UNIVERSITY	MD ..	MOVEMENT RESTRICTION AND FATIGUE IN CANCER SURVIVORS	157
NCRR	5M01RR002635-20	ADLER, GAIL	BRIGHAM AND WOMEN'S HOSPITAL	MA ...	IMMUNONEUROENDOCRINE RESPONSE TO TETANUS TOXOID	4,821

NATIONAL INSTITUTES FOR HEALTH—FUNDING FOR CHRONIC FATIGUE SYNDROME FISCAL YEAR 2004—Continued

[Whole dollars]

IC	Project number	Principal investigator	Institution	State	Project title	Amount
NCRR	5M01RR010710-07	FRIEDBERG, FREDRICK	STATE UNIVERSITY NEW YORK STONY BROOK	NY	PSYCHIATRIC COMORBIDITY IN CHRONIC FATIGUE SYNDROME	159,869
NCRR	5M01RR010710-07	FRIEDBERG, FREDRICK	STATE UNIVERSITY NEW YORK STONY BROOK	NY	WHY DO PEOPLE DROP OUT OF SUPPORT GROUPS FOR CHRONIC FATIGUE SYNDROME?	6,401
NCRR	5M01RR016587-03	HURWITZ, BARRY	UNIVERSITY OF MIAMI-MEDICAL	FL	RBC MASS/AUTONOMIC NERVOUS SYSTEM/INTEGRITY/SYNDROME IN CHRONIC FATIGUE SYNDROME	142,237
NCRR	5P20RR011145-10	FRIEDMAN, THEODORE C	CHARLES R. DREW UNIVERSITY OF MED & SCI.	CA	USE OF VIAGRA TO ALTER SYMPTOMS IN PTS WITH CFS	118,851
NCRR	5P41RR008119-12	TARASOV, SERGEY G	UNIVERSITY OF MARYLAND BALT PROF SCHOOL	MD	SPECT & DNA BINDING OF NAPHTHYLMIDO IMIDAZOACRIDONE WMC79 & RELATED COMPOUND.	43,966
NCRR	5P51RR000168-43	MADRAS, BERTHA K	HARVARD UNIVERSITY (MEDICAL SCHOOL)	MA	MOLECULAR TARGETS OF THE ANTI-NARCOLEPTIC DRUG MODAFINIL	14,843
NCRR	5R13RR017508-03	LAKOWICZ, JOSEPH R	UNIVERSITY OF MARYLAND BALT PROF SCHOOL	MD	CFS COURSE ON FLUORESCENCE SPECTROSCOPY: MICROSCOPY, DATA ANALYSIS, FLUOROMETRY.	4,084
TOTAL NCRR						801,000
OD	1R01HD43301-02	TAYLOR, RENEE	UNIVERSITY OF ILLINOIS, CHICAGO	IL	CFS	400,000
TOTAL OD						400,000
GRAND TOTAL						5,482,957

NATIONAL INSTITUTES FOR HEALTH—FUNDING FOR CHRONIC FATIGUE SYNDROME FISCAL YEAR 2005

[Whole dollars]

IC	Project number	Principal investigator	Institution	State	Project title	Amount
NHLBI	5 R01 HL045462	COLLINS, TUCKER O	CHILDREN'S HOSPITAL BOSTON	MA	TRANSCRIPTIONAL REGULATION OF E-SELECTIN	\$177,750
NHLBI	5 R01 HL054926	ISCHIROPOUL OS, HARRY	CHILDREN'S HOSPITAL OF PHILADELPHIA	PA	REACTIVE SPECIES IN VASCULAR DISEASE-INJURY MECHANISMS.	170,000

NHLBI	5 R01 HL055591	LOMASNEY, JON W	NORTHWESTERN UNIVERSITY	IL	MOLECULAR BASIS FOR PROTEIN-PHOSPHOLIPID INTER-ACTION.	148,500
NHLBI	5 R01 HL056850	CLEMMONS, DAVID R	UNIVERSITY OF NORTH CAROLINA CHAPEL.	NC	MECHANISMS BY WHICH IGF-I STIMULATES SMOOTH MUSCLE CELLS.	209,541
NHLBI	5 R01 HL059459	FREEMAN, ROY	BETH ISRAEL DEACONESS MEDICAL	MA	ORTHOSTATIC INTOLERANCE IN CFS	403,952
NHLBI	5 R01 HL061388	CRANDALL, CRAIG G	UNIVERSITY OF TEXAS SW MED	TX	HEAT STRESS AND CIRCULATORY CONTROL	47,164
NHLBI	5 R01 HL067422	CRANDALL, CRAIG G	UNIVERSITY OF TEXAS SW MED	TX	SKIN COOLING TO IMPROVE ORTHOSTATIC TOLERANCE	131,500
NHLBI	5 R01 HL070215	CALDWELL, ROBERT W	MEDICAL COLLEGE OF GEORGIA (MCG).	GA	ENDOTHELIAL CELL DYSFUNCTION IN OXIDATIVE STRESS MODELS.	125,562
TOTAL NHLBI						1,413,969
NINDS	5Z01NS002979-07	DAVID, GOLDSTEIN	NINDS INTRAMURAL RESEARCH PROGRAM	MD	CLINICAL NEUROCARDIOLOGY: CATECHOLAMINE SYSTEMS IN STRESS AND DISEASE.	559,424
NINDS	9L3ONS054198-02	FRANTOM, CATHERINE G	LOAN REPAYMENT		NEURO-REHAB MEASUREMENT	3,058
TOTAL NINDS						562,482
NIAID	5 R01 AI051270-04	TAM, PATRICIA E	UNIVERSITY OF MINNESOTA TWIN CITIES.	MN	VIRAL DSRNA AS A MEDIATOR OF CHRONIC MUSCLE DISEASES.	349,860
NIAID	5 R01 AI054478-03	NATELSON, BENJAMIN H	UNIV OF MED/DENT OF NU-NU MEDICAL SCHOOL	NU	SLEEP AND CYTOKINES IN CHRONIC FATIGUE SYNDROME	673,289
NIAID	1 R01 AI055735-01A2	JASON, LEONARD A	DE PAUL UNIVERSITY	IL	RISK FACTORS ASSOCIATED WITH CFS AND CF PROGNOSIS.	541,703
NIAID	5 R01 AI056014-02	SULLIVAN, PATRICK F	UNIVERSITY OF NORTH CAROLINA CHAPEL HILL.	NC	MICROARRAYS & PROTEOMICS IN MZ TWINS DISCORDANT FOR CFS.	518,667
TOTAL NIAID						2,083,519
NICHD	R01HD043301-03	TAYLOR, RENE E R	UNIVERSITY OF ILLINOIS AT CHICAGO.	IL	CHRONIC FATIGUE SYNDROME IN ADOLESCENTS	268,159
TOTAL NICHD						268,159
NIAIMS	5-R01-AR-47678-04	BUCHWALD DEDRA S	UNIVERSITY OF WASHINGTON	WA	ARE FIBROMYALGIA AND CHIARI I MALFORMATION RELATED?	127,983
TOTAL NIAIMS						127,983

NATIONAL INSTITUTES FOR HEALTH—FUNDING FOR CHRONIC FATIGUE SYNDROME FISCAL YEAR 2005—Continued
[Whole dollars]

IC	Project number	Principal investigator	Institution	State	Project title	Amount
NIMH	5K23MH001961-05	FRIEDBERG, FRED	STATE UNIVERSITY NEW YORK STONY BROOK	NY	PSYCHIATRIC COMORBIDITY IN CHRONIC FATIGUE SYNDROME.	157,316
TOTAL, NIMH						157,316
NCRR	1M01RR020359-01	BARANIUK, JAMES N	CHILDREN'S RESEARCH INSTITUTE.	DC	RHINITIS IN CHRONIC FATIGUE SYNDROME (CFS)	3,236
NCRR	2M01RR000052-44	SCHWARTZ, CINDY	JOHNS HOPKINS UNIVERSITY	MD	MOVEMENT RESTRICTION AND FATIGUE IN CANCER SURVIVORS.	1,246
NCRR	2P20RR011145-11	FRIEDMAN, THEODORE C	CHARLES R. DREW UNIVERSITY OF MED & SCI.	CA	USE OF VIAGRA TO ALTER SYMPTOMS IN PTS WITH CFS	19,782
NCRR	2P41RR002305-21A1	MCCULLY, KEVIN	UNIVERSITY OF PENNSYLVANIA	PA	CHRONIC FATIGUE SYNDROME	16,453
NCRR	5M01RR000037-45	SMITH, MARK	UNIVERSITY OF WASHINGTON	WA	THE EFFECT OF PARENTAL CHRONIC FATIGUE SYNDROME ON OFFSPRING.	6,418
NCRR	5M01RR000042-45	WILLIAMS, DAVID A	UNIVERSITY OF MICHIGAN AT ANN ARBOR.	MI	SUBJECT REGISTRY: INTERDISCIPLINARY STUDIES OF CHRONIC MULTI-SYMPTOM ILLNESSES.	77,197
NCRR	5M01RR000046-45	LIGHT, KATHLEEN C	UNIVERSITY OF NORTH CAROLINA CHAPEL HILL	NC	FACTORS IN ARTHRITIS, CFS, FIBROMYALGIA & TEMPOROMANDIBULAR DISORDERS.	17,907
NCRR	5M01RR000048-44	TAYLOR, RENEE	NORTHWESTERN UNIVERSITY	IL	A PROSPECTIVE STUDY OF CHRONIC FATIGUE SYNDROME IN ADOLESCENTS.	26,247
NCRR	5M01RR000071-42	MATHEW, SANJAY	MOUNT SINAI SCHOOL OF MEDICINE OF NYU.	NY	MRS NEUROMETABOLITES IN CHRONIC FATIGUE SYNDROME, GENERALIZED ANXIETY DISORDER.	10,871
NCRR	5M01RR010710-08	FRIEDBERG, FREDRICK	STATE UNIVERSITY NEW YORK STONY BROOK	NY	PSYCHIATRIC COMORBIDITY IN CHRONIC FATIGUE SYNDROME.	48,251
NCRR	5M01RR010710-08	FRIEDBERG, FREDRICK	STATE UNIVERSITY NEW YORK STONY BROOK	NY	WHY DO PEOPLE DROP OUT OF SUPPORT GROUPS FOR CHRONIC FATIGUE SYNDROME?	42,683
NCRR	5M01RR016587-04	HURWITZ, BARRY	UNIVERSITY OF MIAMI-MEDICAL	FL	RBC MASS/AUTONOMIC NERVOUS SYSTEM/INTEGRITY/SYNDROME IN CHRONIC FATIGUE SYNDROME.	28,827
NCRR	5P41RR0080119-13	NOWACZYK, KAZIMIERZ	UNIVERSITY OF MARYLAND BALT PROF SCHOOL.	MD	CFS COMPUTERS	20,687
NCRR	5P51 RR000168-44	MADRAS, BERTHA K	HARVARD UNIVERSITY (MEDICAL SCHOOL).	MA	MOLECULAR TARGETS OF THE ANTI-NARCOLEPTIC DRUG MODAFINIL.	120,481

NCRR	5R13RR017508-04	LAKOWICZ, JOSEPH R	UNIVERSITY OF MARYLAND BALT PROF SCHOOL	MD ..	CFS COURSE ON FLUORESCENCE SPECTROSCOPY: MICROS- COPY, DATA ANALYSIS, FLUOROMETRY.	4,207
TOTAL NCRR	444,493
OD	1R01HD43301-03	TAYLOR, RENEE	UNIVERSITY OF ILLINOIS AT CHI- CAGO	IL	CFS	300,000
OD	1R01A055735-01A2	JASON, LEONARD	DE PAUL UNIVERSITY	IL	CFS	100,000
TOTAL OD	400,000
TOTAL, NIH	5,457,921

Question. NIH is expected to announce later this month the awards made in response to the 7/14/05 RFA for CFS. Will the studies funded under this RFA yield a true increase in the level of NIH research funding for CFS?

Answer. Yes. The 7 new grants funded will infuse an additional several million dollars into the bottom line for CFS funding that has remained relatively constant in the \$5.5–\$6 million range over the past years. A projected \$2 million is derived from the redirected funds of the ORWH budget to fund and co-fund studies through the ICs. The remainder will be provided by the NIAAA, NIAMS, NIEHS, and NINDS. Additionally, individual letters sent from the Tans-NIH Working Group for Research on Chronic Fatigue Syndrome encouraged the unsuccessful applicants to revise and submit their proposals under the standing CFS Program Announcement. Many have been in touch for advice and plan to resubmit. The announcement resulted in increased interest from many researchers who had not previously conducted research on CFS. They are now aware that NIH interest in CFS is broad based and that many disciplines can contribute. It is expected that this RFA, information on the new website, and contacts established with members of the CFSWG will lead to a further increase in investigator initiated submissions.

Question. You have been a strong advocate for more centralized power and discretion within the NIH Office of the Director for the Roadmap Initiative to identify major opportunities and gaps in research that no single institute at NIH can tackle alone but that the agency as a whole must address. CFS is a complex illness that affects the brain and multiple body systems and thus is an example of a condition that must be addressed by multiple institutes. The CDC is expected to announce that CFS affects more than four million adults in the United States. In 1999, responsibility for CFS was moved to the Office of the Director. What progress in NIH's approach to the study of CFS has been made since this move?

Answer. Tremendous progress has been and will continue to be made in pursuing and further stimulating CFS research. This is accomplished through a trans-NIH Working Group for Research on CFS (CFSWG) that is chaired by the Office of Research on Women's Health (ORWH) in the Office of the Director and includes members from 13 different ICs. The CFSWG was established in April 2001 to develop an action plan to enhance the status of CFS research at the NIH and among the external scientific community. The Working Group first issued a program announcement based on recommendations from the Chronic Fatigue Syndrome, State of the Science Conference held in October 2000 that encouraged innovative and interdisciplinary CFS research. The CFSWG updated and reissued this announcement in 2005 based on the results of a second NIH-sponsored scientific workshop. This workshop, Neuro-Immune Mechanisms and Chronic Fatigue Syndrome: Will understanding central-mechanisms enhance the search for the causes, consequences and treatment of CFS?, was held in June 2003. Its proceedings were published in 2004 (NIH Publication No. 04–5497) and disseminated widely among the scientific community. The first issue of the new ORWH Science Series for the Public, informational fact sheets, is also derived from these proceedings. Also based on these proceedings, the ORWH and the CFSWG developed a request for applications (RFA) to explicate how the brain, as the mediator of the various body systems involved, fits into the schema for understanding CFS (RFA OD–06–002). This RFA specifically solicited proposals from multidisciplinary teams of scientists to develop an interdisciplinary approach to the mechanisms involved in CFS in men and women across the life span. Twenty-nine applications were received and are in process. All documents mentioned above as well as complete information about the NIH CFS program are available at <http://orwh.od.nih.gov/cfs.html>. All of the above demonstrate concerted trans-NIH efforts coordinated by an OD program office that is the focal point for research on women's health, ORWH, to engage the scientific community in addressing the many aspects of and increasing knowledge of CFS.

Question. Has the move to the Office of the Director led to any real progress in multidisciplinary research? If so, what specifics can you point to?

Answer. Yes. Collaborative achievements that include the development of an action plan to enhance the status of CFS research at the NIH and the products of this plan, such as trans-NIH Program Announcements, Requests for Applications, Scientific Workshops would not have been possible without the formation of a trans-NIH CFSWG chaired by the ORWH in the Office of the Director. The ORWH has had a long and successful track record for developing and leading interdisciplinary research and training initiatives on women's health and sex and gender factors in human health through its Coordinating Committee for Research on Women's Health (CCRWH), which brings together representatives from every institute and center to facilitate collaborative efforts. Similarly, the CFSWG, supported and led by the ORWH, is composed of representatives from 13 NIH institutes and centers with an interest in facilitating collaborative efforts to invigorate CFS research at the NIH.

Question. How does the current status of CFS research within the NIH serve as a model for progress, based on more centralized authority within the Office of the Director or as a model for multidisciplinary approaches and the Roadmap.

Answer. NIH has made steady progress towards an interdisciplinary approach to CFS through the efforts and function of an OD program office that was established to serve as the NIH focal point for the OD on women's health research. Therefore, the OD, through ORWH, was able to bring together diverse institutes to collaborate effectively in a trans-NIH initiative to enhance research on CFS. The ORWH also contributed staff and budget to these expanded research activities. This ORWH effort for CFS serves as an example of how an office within the OD can facilitate trans-NIH scientific initiatives that manifest real progress in research.

QUESTIONS SUBMITTED BY SENATOR HERB KOHL

ALZHEIMER'S DISEASE

Question. In April, the National Center for Health Statistics reported that the life expectancy of Americans has risen to 78 years—the highest it has ever been. However, they also reported that the death rate from Alzheimer's disease is increasing among the top 10 causes of death in the United States. In light of the fact that the Baby Boom generation is entering the age of highest risk for Alzheimer's, shouldn't NIH be increasing, rather than reducing, its investment in Alzheimer's research?

Answer. It should be noted that our fiscal year 2007 funding level for Alzheimer's disease is an estimate and reflects a reduction that is comparable to the reductions in the total budgets of the NIH ICs supporting research in this important area. At this time, it is not possible to be precise as to where available funding will be allocated. Funding decisions will be based on public health need, scientific and technological opportunity, and the peer review of research applications.

As the Senator points out, with current trends, Alzheimer's disease will become an increasingly critical public health concern over the coming decades. To reverse this trend, it is critical that we explore all promising avenues of discovery and promote the translation of research results into interventions for the successful prevention, detection, diagnosis, and treatment of Alzheimer's disease. Alzheimer's disease research continues to be a high priority for NIH, and scientific opportunities in this area will be actively pursued within available resources.

EPILEPSY

Question. As you know, for years I have pushed NIH to work harder to develop better treatments and a cure for epilepsy. I have supported efforts by the National Institute of Neurological Disorders and Stroke to fund epilepsy research. However, many experts think we need a broader approach, with greater collaboration between NINDS and the National Institute on Mental Health, the National Institute on Child Health and Human Development, and other Institutes. What are you doing to guarantee that multi-Institute studies on epilepsy are developed and funded in the coming year?

Answer. As the lead NIH Institute for epilepsy research, the National Institute of Neurological Disorders and Stroke (NINDS) coordinates epilepsy research efforts through the InterAgency Epilepsy Working Group. The Epilepsy Working Group is composed of scientific program staff from the NINDS, eight other Institutes, including the National Institute of Mental Health (NIMH), the National Institute of Child Health and Human Development (NICHD), and staff members from the Centers for Disease Control and Prevention. The Working Group facilitates coordination and collaboration among NIH Institutes. For example, NINDS and NIMH Epilepsy Working Group members collaborated with the American Epilepsy Society to sponsor an international workshop in May 2005 on treatment of nonepileptic seizures (NES), a neuropsychiatric seizure disorder. As a result of this meeting, the NIMH and the NINDS issued a request for applications on "Collaborative Research on Mental and Neurological Disorders."

This initiative focused on co-morbidities between mental health and neurological disorders, including epilepsy.

The NINDS and the NICHD have a long history of collaboration on epilepsy research. The NICHD funds the Mental Retardation Research Centers Program, a network of regional centers developed for research on mental retardation and related aspects of human development, including epilepsy. Many of the Centers also provide infrastructure for NINDS-supported epilepsy research projects. Both Institutes fully expect this successful collaboration to continue in the future.

The NIMH, NICHD, and NINDS also collaborate in funding the Autism Research Network (ARN). The ARN is made up of eight collaborative research centers that focus on the causes, diagnosis, early detection, prevention, and treatment of autism. One of the network studies, "A Longitudinal Assessment of Behavior Problems, Puberty, and Epilepsy" is designed to investigate which children with autism develop seizures and whether there are changes in behavior that either precede or follow the development of seizures.

Question. As you know, NINDS held a successful epilepsy conference in 2000, where research benchmarks were developed and used to create a research agenda in epilepsy. It's my understanding that NINDS is planning a follow-up conference on Curing Epilepsy in March 2007. Will you ensure that representatives from other Institutes participate in the 2007 conference? What steps will you take after the conference to ensure that collaborative research is pursued in order to have the greatest impact for epilepsy patients?

Answer. The NINDS has invited all the organizations represented on the Inter-Agency Epilepsy Working Group (IAEWG) to participate in planning and co-sponsoring the Curing Epilepsy 2007 conference. Co-morbidities, such as cognitive and psychological issues in children and adults with epilepsy, will be one of the major themes of the conference. Epilepsy co-morbidities often include behavioral problems, learning and memory difficulties, and depression. The NINDS expects that the conference will draw attention to the importance of these issues and will stimulate interdisciplinary investigation into the causes, treatment and prevention of epilepsy and its co-morbidities. The IAEWG will also consider the potential for collaborative activities in response to any recommendations that result from the Curing Epilepsy 2007 conference.

AGE-RELATED MACULAR DEGENERATION

Question. You have publicly cited as an NIH "breakthrough" the discovery of a gene strongly associated with age-related macular degeneration (AMD). As you know, AMD is the leading cause of blindness in the United States, especially among our seniors, robbing them of their independence and quality of life. What does this finding mean for new treatments to stop or reverse this blinding eye disease? How will the National Eye Institute follow up on this exciting breakthrough when the President's budget proposes to cut NEI funding?

Answer. National Eye Institute-sponsored investigators have made considerable progress since the recent discovery of the complement factor H (CFH) gene in age-related macular degeneration (AMD). NEI intramural researchers are initiating a phase I clinical trial to evaluate anti-inflammatory agents that may inhibit damaging immune responses potentially resulting from alterations in the CFH gene. NEI extramural and NIH intramural scientists discovered that alterations in a second gene in the inflammatory pathway, complement factor B, are also associated with AMD. Variations in these two genes can predict the clinical outcome in 74 percent of individuals with AMD. In addition, the NEI launched a new research initiative to further investigate the role of inflammation in AMD and other common eye diseases such as diabetic retinopathy and uveitis.

IRRITABLE BOWEL SYNDROME

Question. For the last several years, the Appropriations Committee has asked the National Institute of Diabetes and Digestive and Kidney Diseases to develop a strategic plan for research into Irritable Bowel Syndrome. NIDDK has explained that the Institute [is] creating an overall digestive disease action plan and that IBS will be a significant part of it. Can you update us on NIDDK's progress on the digestive disease plan and explain how much attention IBS will receive?

Answer. The NIH established a National Commission on Digestive Diseases in August 2005, based on the shared interest of the NIH and the Congress in advancing research on digestive diseases. One of the Commission's primary purposes is to develop a Long-Range Research Plan for Digestive Diseases, which will include plans for stimulating research on functional gastrointestinal (GI) and motility disorders such as irritable bowel syndrome (IBS). Within the NIH, the NIDDK has lead responsibility for digestive diseases research and supports a research portfolio in IBS and other types of functional GI and motility disorders. The NIDDK is providing leadership and support for this federally chartered Commission.

As NIH Director, I appointed members of the Commission after a broad call for nominees with diverse scientific, professional, and personal experiences related to digestive diseases from within the academic and medical research and practice communities, patient and patient advocacy community, and the NIH and other Federal health agencies. The perspective of individuals with personal or professional interest

in IBS and other types of functional GI and motility disorders is represented within the Commission.

Commission members recently convened for their first meeting on June 12, 2006, and are currently finalizing topics for chapters of the Research Plan, one of which is expected to focus on IBS and related GI motility disorders research. The ultimate goal of the Commission's Research Plan is to improve the nation's health through advancing research on digestive diseases, such as IBS. The Research Plan will include: (1) information on the burden of disease on individuals and society; (2) examples of research advances that are generating new knowledge vital to understanding, treatment, and prevention; and (3) compelling opportunities for future NIH-funded research, which offer promise for reducing the burden of disease. This Research Plan will recommend promising research directions relevant to IBS and other types of functional GI and motility disorders, which will help guide the NIDDK, the NIH, and the investigative and lay community in the pursuit of the most productive research avenues.

The Commission will rely on broad stakeholder input from members of the digestive diseases community to inform the Research Plan throughout its development. For example, Commission members are currently establishing Working Groups composed of individuals with expertise related to specific areas of digestive diseases research, who will provide input necessary for crafting a well-informed Research Plan. One of these Working Groups is expected to focus on functional GI and motility disorders, such as IBS, in addition to potential overlapping and synergistic efforts in this area on the part of other Working Groups. Other opportunities for broad stakeholder input into the Commission's activities will include public Commission meetings and an open comment period for public input on the draft Research Plan. Additional information on the Commission's ongoing activities can be found on its website at: <http://NCDD.niddk.nih.gov>.

CONCLUSION OF HEARINGS

Senator SPECTER. So thank you for what you are doing. We appreciate your thanks to us, and we are going to do more and we ask you to do more. That concludes our hearings.

[Whereupon, at 10:14 a.m., Friday, May 19, the hearings were concluded, and the subcommittee was recessed, to reconvene subject to the call of the Chair.]

**DEPARTMENTS OF LABOR, HEALTH AND
HUMAN SERVICES, EDUCATION, AND RE-
LATED AGENCIES APPROPRIATIONS FOR
FISCAL YEAR 2007**

U.S. SENATE,
SUBCOMMITTEE OF THE COMMITTEE ON APPROPRIATIONS,
Washington, DC.

DEPARTMENT OF LABOR
OFFICE OF THE SECRETARY

THAD COCHRAN, MISSISSIPPI, CHAIRMAN

TED STEVENS, ALABAMA
ARLEN SPECTER, PENNSYLVANIA
PETE V. DOMENICI, NEW MEXICO
CHRISTOPHER S. BOND, MISSOURI
MITCH MCCONNELL, KENTUCKY
CONRAD BURNS, MONTANA
RICHARD C. SHELBY, ALABAMA
JUD GREGG, NEW HAMPSHIRE
ROBERT F. BENNETT, UTAH
LARRY CRAIG, IDAHO
KAY BAILEY HUTCHISON, TEXAS
MIKE DEWINE, OHIO
SAM BROWNBACK, KANSAS
WAYNE ALLARD, COLORADO

ROBERT C. BYRD, WEST VIRGINIA
DANIEL K. INOUE, HAWAII
PATRICK J. LEAHY, VERMONT
TOM HARKIN, IOWA
BARBARA A. MIKULSKI, MARYLAND
HARRY REID, NEVADA
HERB KOHL, WISCONSIN
PATTY MURRAY, WASHINGTON
BYRON L. DORGAN, NORTH DAKOTA
DIANNE FEINSTEIN, CALIFORNIA
RICHARD J. DURBIN, ILLINOIS
TIM JOHNSON, SOUTH DAKOTA
MARY L. LANDRIEU, LOUISIANA

J. KEITH KENNEDY, STAFF DIRECTOR
TERRENCE E. SALVAIN, MINORITY STAFF DIRECTOR

United States Senate

COMMITTEE ON APPROPRIATIONS
WASHINGTON, DC 20510-6025
<http://appropriations.senate.gov>

June 16, 2006

Honorable Elaine Chao
Secretary
U.S. Department of Labor
Washington, D.C.

Dear Madam Secretary,

Due to the press of Senate business and the particularly heavy schedule of the Judiciary Committee, it has been necessary to postpone, several times, your appearance before the Subcommittee on Labor, Health and Human Services and Education. At this late date, neither your schedule nor mine will permit a hearing in time to obtain the information needed to mark-up the Labor-HHS bill.

I am therefore requesting that you answer, in writing, the enclosed series of questions pertaining to the Department of Labor's fiscal year 2007 budget request. Please provide your responses not later than July 7, 2006. "

My best,

Sincerely,



Arlen Specter
Chairman
Subcommittee on Labor, Health and Human
Services and Education Appropriations

[The following questions were submitted to be answered for the record:]

QUESTIONS SUBMITTED BY SENATOR ARLEN SPECTER

MINE SAFETY

Question. Congress has now passed bi-partisan mine safety legislation that contained many of the provisions in a bill I introduced on February 16, 2006. Congress has also passed a pending supplemental appropriations bill containing \$35,600,000 to augment inspections of coal mines and to expand research to develop mine safety technology. How do you intend to implement these authorization and appropriation measures? What additional appropriations are necessary to fully implement the new authorization?

During the hearing this Subcommittee held on January 23, 2006, on the Sago Mine disaster, I questioned the policy of the requiring mine representatives to be present during accident investigation interviews with miners. Although the legislation I introduced would prohibit this practice, it was not included in the consensus bill reported last week. Do you support such a provision?

Answer. \$25.6 million of the \$35.6 million contained in the supplemental appropriation was appropriated to MSHA. The supplemental appropriation contains a provision requiring MSHA to submit a spending plan for these funds to the appropriations committees by July 15, 2006, and MSHA will comply with this provision. The remaining \$10 million in supplemental funding was appropriated to NIOSH for expansion of research and mine safety technology, therefore NIOSH is the appropriate entity to answer questions regarding their plans for the use of those funds. With regard to additional appropriations necessary to fully implement the MINER Act, the MINER Act contains authorization for new grant programs but no funding for these programs has been appropriated. Many of the new MINER Act provisions do not require any additional funding. For example, the increase of the maximum civil penalty for flagrant violations and the implementation of minimum penalties for unwarrantable citations and orders, as well as the provision requiring every mine to have an Emergency Response Plan do not require any increases in funding.

With regard to MSHA accident investigations, the Mine Act gives MSHA discretion to determine who may be present during accident investigation interviews with miners and other persons who may have relevant information. As you are aware, MSHA's longstanding past practice regarding interviews has generally included participation by the mine operator and the representative of miners. However, we have come to the conclusion that this process should be changed to conform to the process used by virtually all other law enforcement investigative agencies. We believe that witness interviews should be conducted with only federal, and where applicable, state authorities. Of course, witnesses would continue to have the option of having a personal representative of their choosing present during the interview. We believe that the time proven technique of interviewing witnesses separately and without additional persons present is the best method of eliciting useful information without fear of intimidation, and minimizes the ability of witnesses to modify their testimony in light of the knowledge gained from other witnesses. In fact, recent experience has demonstrated that the presence of third-parties could compromise the investigation, make witnesses less likely to cooperate, and result in premature release of information before all witness interviews are complete. Thus, we agree that participation in interviews by non-government personnel should be limited to a personal representative of the witness. Of course, MSHA will continue its practice of releasing all witness transcripts, except those requested under the Mine Act to be confidential, once the investigation has reached a stage where release would not impede or interfere with the investigation.

JOB CORPS FUNDING

Question. It has been more than 45 calendar days of continuous session of the Congress since the President proposed rescinding \$75 million of Job Corps construction and renovation funds. Have these funds now been released as required by the Congressional Budget and Impoundment Control Act?

Answer. The \$75 million in Construction, Rehabilitation, and Acquisition funds were not withheld from obligation, as noted in our May 30, 2006 letter to GAO on this matter, and remain available for obligation by the Office of Job Corps.

Question. Your budget proposed to cut \$62,578,000 from the Job Corps budget for program year 2007, which would result in 3,614 fewer students enrolled than in 2005. This would reduce funding, on inflation-adjusted basis, 8.5 percent below the level in 2005. How far below capacity would this put the 122 existing Job Corps centers?

Answer. With the requested 2007 operating budget of \$1,401,602,000, Job Corps will be able to maintain 42,863 year-around training slots, which represents 95.5 percent of the peak level that could be accommodated by our physical infrastructure.

REINTEGRATION OF YOUTHFUL OFFENDERS

Question. Your budget once again zeroes out the program I was instrumental in creating, for training and employing of youthful offenders. Even after last November's conference agreement restored \$49 million for this program, the Administration immediately offered it up as an offset to help pay for December's Katrina supplement. Do you think this was an appropriate way to respond?

Answer. The impacts of the Katrina and Rita hurricanes were unprecedented and the Administration carefully prioritized the use of available resources across government to fund relief and recovery efforts. The Youth Offender appropriation was only one of many offsets the Administration presented to Congress, and this is consistent with the Administration's proposal in the fiscal year 2007 and previous budgets to replace the Responsible Reintegration of Young Offenders program with the Prisoner Reentry Initiative, thereby increasing the program's overall scope and reach.

ELIMINATION OF MIGRANT JOB TRAINING

Question. Both the House and the Senate appropriations committees have repeatedly rejected your proposal to eliminate the Migrant and Seasonal Farmworkers Program under the Workforce Investment Act. I think it's fair to say that Congress recognizes that it is unrealistic to expect states and localities to be responsible for a unique and difficult-to-serve migratory population that, from their point of view, is "here today and gone tomorrow." It is also unfair to shift this burden to states when you are proposing to reduce the already limited job training resources that states have to serve their eligible local residents. If Congress understands this, why doesn't the Department?

Answer. The Administration's fiscal year 2007 Budget proposal seeks to tap the workforce investment system's potential to serve more migrant and seasonal farmworkers by providing job training services to them through the One-Stop Career Center system, and turning to other, appropriate agencies to provide supportive services, housing, and other related assistance. Currently, the section 167 program provides employment and training services to only 10,000 of an estimated two million farmworkers, which demonstrates the need for a wider system approach.

The Administration believes that providing services to farmworkers through the One-Stop system will increase the number served and have a positive employment and earnings impact on those who receive services.

IMPACT OF JOB TRAINING CUTS

Question. Your budget is based on the assumed enactment of a new Workforce Investment Act reauthorization proposal calling for Career Advancement Accounts, to be run through a consolidated workforce system, cutting nearly \$700 million. Until the authorization legislation is changed, this Committee acts on the basis of extending current law. In the absence of law change, what impact will your budget proposals have on existing programs for youth, adults, dislocated workers, and the Employment Service? For example, the Pennsylvania Association of Workforce Investment Boards estimates the President's Budget would result in a 17 percent cut from current levels for the youth, adult and dislocated worker block grants. Do I have your assurance that you will not proceed administratively to implement proposals such as consolidated Career Accounts without Congressional approval?

Answer. The President's Budget request does assume enactment of the Career Advancement Account (CAA) proposal, which would reduce overhead and administrative costs and focus more funding on training, thereby tripling the number of individuals receiving job training through the workforce investment system.

In the absence of any legislation passed by Congress, states will continue to operate Workforce Investment Act programs and the Employment Service as currently authorized. The appropriation level provided by Congress is a separate issue from job training reform. We feel that CAAs are a more effective approach than the current workforce investment system, regardless of the funding level provided by Congress.

Several states and local areas have expressed interest in piloting CAAs. We will work with these areas to develop a limited pilot that can be carried out under current law. However, statutory changes are necessary to achieve all of the reforms envisioned under the CAA proposal.

WORKFORCE TRAINING CUTS

Question. Your budget for workforce programs contains cuts of \$506 million for state grant programs, while increasing funding under national control by \$107 million. How does this square with your legislative proposal to shift greater control of resources to the States?

Answer. The President's fiscal year 2007 Budget proposes a minimal increase for programs under "national control." The only activity that falls under this category that is proposed for additional funding is Unemployment Insurance National Activities, whereby an increase of \$600,000 is requested to pay for activity related to processing separation documents and unemployment claims of former military service personnel.

Furthermore, the fiscal year 2007 Budget request proposes initiatives that give greater control of funding to states and local areas. The Career Advancement Account proposal promotes state and local flexibility by streamlining and strengthening the One-Stop Career Center system and removing or simplifying statutory requirements that create rigidity and hinder flexibility in providing education and training opportunities to American workers. Also, the Administration included a streamlined program structure in its Older Americans Act reauthorization proposal, which would give states greater control over the Senior Community Service Employment Program (SCSEP) funds.

ASBESTOS EXPOSURE

Question. Madame Secretary, the fiscal year 2006 appropriation contained \$2 million for the Employment Standards Administration to facilitate the expeditious startup of a system to resolve the claims of injury caused by asbestos exposure. How are these funds being used to shorten the lead-time for implementation of pending asbestos legislation?

Answer. If the Asbestos legislation is enacted as currently written, the Department of Labor will be expected to manage a new and very substantial national benefits program involving the disbursement of billions of dollars in compensation to hundreds of thousands of individual asbestos claimants. The proposed time frame for implementing this legislation is extremely short, requiring immediate preparatory work and the up-front expenditure of resources to ensure that payments can begin being made to compensable claimants as quickly as possible.

Given the status of the pending legislation, the \$2 million is being used to analyze the proposed legislation and plan how to implement it in the event that it is passed. In the next phase, funding will be used for initial program start-up expenses in the areas of program design, acquisition of specialized expertise, technology, and infrastructure.

OSHA PENALTIES FOR ASBESTOS VIOLATIONS

Question. I have introduced legislation (S. 668) to subject employers who willfully violate OSHA asbestos standards to fines at levels set by the Uniform Criminal Code as well as imprisonment of up to five years, or both. Currently OSHA provides for criminal penalties only in those cases where a willful violation of standards results in the death of a worker within six months after the violation is discovered. Do you agree that stronger enforcement action is needed against parties that violate OSHA asbestos enforcement rules?

Answer. Currently, the OSH Act provides for criminal fines and imprisonment of up to six (6) months against an employer only where the employer's willful violation of a standard caused the death of an employee. In addition, criminal penalties exist against employers who make false statements to OSHA investigators or who unlawfully interfere with OSHA investigations. S. 668 provides that any willful violation of a standard issued under OSH Act section 6 with respect to control of occupational exposure to asbestos is punishable by fines under section 3571 of Title 18, United States Code, and imprisonment in the case of a first offense, of up to five years. While we agree that occupational exposure to asbestos is a very serious health issue, we believe the current OSH Act and penalty structure provide the means and flexibility to address instances where penalties are warranted.

IMMIGRATION BILL

Question. The Senate passed immigration legislation, S. 2611, contains a provision requiring the Secretary of Labor to certify that no United States workers are available for a specified position before employers can hire an alien for the job. Do you support this provision, and does your Department have sufficient resources to administer it?

Answer. The Department supports the need to enact comprehensive immigration reform that creates a guest worker program and enhances the security of our borders. In his various speeches on immigration reform, the President has repeatedly noted that foreign workers should be allowed to take only those jobs that no U.S. worker is willing or available to perform. To implement this important program design feature, the Department will need to either establish a labor market test for domestic worker interest or create a mechanism whereby employers can attest that they have tested the labor market and been unable to find a U.S. worker to fill the job. If an attestation system is created, the Department would randomly audit employer attestations to ensure program integrity. We agree that the S. 2611 provision is consistent with the President's position and we support it accordingly. The administration will work with Congress as immigration legislation moves forward to ensure that the need for resources is addressed.

Question. Your Department has the responsibility to prevent employer exploitation of undocumented workers, by enforcing minimum wage and overtime laws. To what extent is this effort discouraging illegal immigration?

Answer. The strong enforcement of basic labor standards for all employees weakens the incentive to hire undocumented workers. Although it is difficult to quantify the extent to which labor standards enforcement deters or dissuades employers from hiring undocumented workers, most studies on the impact of illegal immigration acknowledge the importance of such enforcement as a key component in an overall strategy for addressing the problem.

Question. What actions do Labor Department inspectors take when they come across evidence that a business unlawfully employs illegal immigrants?

Answer. When the Wage and Hour Division (WHD) performs an investigation a complaint-based investigation, it does not seek evidence of the complainant's immigration status. WHD instituted this policy to avoid discouraging complaints from undocumented workers who might otherwise be reluctant to complain to WHD because of their immigration status.

However, WHD investigators do perform directed investigations (non-complaint cases) to determine employers' compliance with their employment eligibility verification obligations (Forms I-9). In cases where it appears that violations have been committed, WHD refers the matter to DHS pursuant to a Memorandum of Understanding.

MEDICAL LEAVE PROGRAM

Question. At your last appearance before this Committee on March 15, 2005 you stated no final decision has been made with respect to revising regulations implementing the Family and Medical leave Act. What progress has been made addressing concerns of workers and employers that have resulted in so many lawsuits on the interpretation of when employers are eligible for leave under the law?

Answer. The Department continues to review the issues raised by the Supreme Court's decision in *Ragsdale v. Wolverine World Wide, Inc.*, as well as other court decisions, and the possibility of revisions to the FMLA regulations remains an item on the Department's regulatory agenda. No final decisions have yet been reached as to what, if any, changes might actually be proposed. If changes are proposed, the public will be provided ample opportunity to comment through the formal notice and comment rulemaking process.

RE-ALLOCATION OF UNSPENT FUNDS

Question. Your budget proposed bill language that would take money away from states that have more than 30 percent unspent job training funds, yet you do not propose applying this principle to Dislocated Worker national reserve funds, which currently have unspent funds exceeding 50 percent. What is your justification for this?

Answer. The Department always obligates all National Reserve monies to states during the program year for which such money was appropriated. Any unspent funds are unspent at the state and local level, not at the national level. This indicates that even more funds are available for expenditure by states and grantees.

RAPID RESPONSE FUNDS

Question. Currently, states use rapid response funds to provide immediate service to workers affected by a mass layoff, often before the workers are even laid off. Under your legislative proposal, states will need to apply to the Employment and Training Administration for rapid response funds as events occur. What are the reasons for keeping these funds at the national level, and having states apply for them each time they are faced with mass layoffs?

Answer. The Department does not contemplate that a state would have to apply for funds each time there is a mass layoff or to only sporadically fund a state rapid response coordinator. Early intervention to provide information and assistance to workers to decrease the amount of time between actual layoff and re-employment is a key principle of the dislocated worker program. Rapid response is a key element of this early intervention strategy.

States could demonstrate need and apply for rapid response funds at the beginning of the program year or throughout the program year. We will not propose that a state be required to submit an application for funding each time a dislocation event occurs.

In spite of all the good work that has been done over the past fifteen years with dislocated worker rapid response funds, the Department has found that most company executives do not know about the type and quality of assistance available to them and their employees when closures or layoffs are contemplated. They have also reported that where they have layoffs in several states simultaneously, the levels and quality of assistance varies dramatically. ETA, in collaboration with state and local partners, has undertaken several initiatives in the auto, textile and defense industries recently to try to integrate services and develop more consistency. We believe a nationally-coordinated approach to delivering rapid response assistance by states can help bring the services to more workers and employers.

The proposed mechanism will assist both the Department and the states to better manage scarce taxpayer resources by directing the bulk of the funds to the areas of need. For example, not all states experience major layoffs every year. Analyses of dislocated worker program expenditures reported by states have shown that the funds reserved for rapid response are consistently under-expended. In the aggregate, the rapid response carry-in funds from program year 2003 to 2004, and from 2004 to 2005, was \$136.7 million and \$166 million, respectively. Through March 31, 2006, states reported accrued expenditures of just over \$176 million of a total available of more than \$342.5 million, or 51.4 percent of the total funds available. States are not required to retain the up to 25 percent authorized to be reserved for rapid response activities. They may include a portion of the funds in the amount allocated to local workforce investment boards for core, intensive and training services for dislocated workers, or they may award additional funds from the reserved amount to local areas that experience disasters, mass layoffs, plant closings or other events that precipitate substantial increases (defined by the state) in the number of unemployed workers.

COMMENTS ON CECIL ROBERTS TESTIMONY

Question. Mr. Cecil Roberts, President of the United Mine Workers of America, testified to this Committee that the penalties assessed by the Labor Department are designed to insure that mining remains profitable, even if the conditions are so hazardous the mine should be shut down. Do you believe that keeping a mine operating is more important than the safety of the miners?

Answer. No, we do not believe that keeping a mine operating is more important than the safety of the miners who work in that mine. The Mine Act states in its opening section that "the first priority of all in the coal or other mining industry must be the health and safety of its most precious resource—the miner." That is the premise on which the Mine Act is based and the reason for the existence of MSHA. The Mine Act contains provisions to withdraw miners until the hazard or violation is abated when there is an imminent danger to the health and safety of miners or an unwarrantable failure of an operator to comply with a mandatory health and safety standard. MSHA uses its withdrawal authority vigorously and appropriately.

Under the Mine Act, MSHA has the authority to propose penalties for violations of the Act. MSHA does so in accordance with the six statutory criteria enacted by Congress in the Mine Act, including consideration of the effect of the proposed penalty on the operator's ability to stay in business. Consistent with the Administration's last three budget requests, Congress included a provision in the MINER Act to increase the maximum civil penalty for flagrant violations of the Mine Act to \$220,000. Minimum penalties were also included for unwarrantable failure violations. The Department has announced that MSHA will be revising its regulations and proposing a new penalty formula to raise penalties for mine safety and health violations across the board. These higher penalties should provide a greater incentive to mine operators to comply with MSHA's safety standards.

OLDER WORKER EMPLOYMENT PROGRAM

Question. The Department has launched another national grant competition process for the Senior Community Service Employment Program despite not having the essential performance data that will not be available for new performance goals until September 2006. Since the current law directs that re-competition be conducted for non-performance by a grantee, on what basis do you deem this new round of competition to have sound data for assessing current or future grantee performance or capacity?

Answer. The Department has been collecting performance data since the inception of the program, and has been collecting additional data on the new common performance measures since July 2004.

Furthermore, according to the Title V of the Older Americans Act, competition is not limited to when grantees fail performance measures. Section 514(a) limits the award of SCSEP grants to no more than three years, thus requiring a selection of grantees within three years of the first competition. The issue of whether the Department can compete the SCSEP grants has also been addressed by the courts. The U.S. District Court of the District of Columbia held recently in *Experience Works v. Chao*, 267 F.Supp. 2d 93 (D.D.C. June 17, 2003), "[t]he use of competitive procedures is a time-honored method for obtaining the most highly qualified awardees of government funds, for allowing new and innovative ideas and organizations to receive those funds, and for assuring public confidence in the integrity of the process to distribute government funds."

Finally, the current Solicitation for Grant Applications (SGA) clearly identifies the criteria against which applicants are assessed. All applicants will be rated using a ranking criterion based on points. This SGA requires that responses be thoughtful and reflect a strategic vision.

The SGA evaluation criteria are as follows:

1. Design and Governance—15 points
2. Program and Grant Management Systems—10 points
3. Financial Management System—10 points
4. Program Service Delivery—40 points
5. Performance Accountability—25 points

Question. When the program was competed in 2003, this whole competition process—application, grading and transition—took almost 6 months—including over 6 weeks for transitioning the participants affected. This time the new competition rules are much more complex, yet the whole process has been shortened to 4 months, leaving barely 3 weeks for transition of these vulnerable participants—why the rush to get this done this way this year?

Answer. This year's competition is not rushed. Applicants were given nearly the same amount of time this year as in the 2003 competition to respond to the Solicitation for Grant Applications (SGA). In 2003, grantees were given 90 days to respond to the SGA, a time period which included Christmas. This year, the competition was announced in the Federal Register on March 2, and grantees were given until May 26 to respond, or 85 days.

Further, once grants are awarded, grantees have 2 months in which to transition participants among grantees, a longer transition period than in 2003. As specified in the SGA, the transition period follows a 1-month extension of current grants and will take place August 1-September 30, 2006. This means that the period from publication of the SGA (March 2) until the transition period ends (September 30) is approximately 7 months, 1 month longer than the 2003 competition.

Question. The cost of transitioning thousands of participants nationwide among old and new sponsors will be significant. Subsequent to publication of the SGA in the Federal Register, the DOL website was amended to say, "Transition cost should be submitted as an integral part of the budget and reflected on the other' cost category with a narrative explanation. Can you assure the Committee that services to enrollees will not be diminished as a result of incurred transitions costs?

Answer. All current grantees were required to build transition costs into their budgets in the 2003 competition, and all applicants under the 2006 competition have also budgeted for transition costs. Further, the Department is prepared to assist grantees with additional costs associated with the transition, as it did following the transition after the 2003 competition. Program Year 2004 recaptured funds are available for this purpose.

At the time of the 2003 competition, many participants and grantees were concerned about the transition effects upon participants. The Department can say with authority that every single participant was transitioned successfully. Competition does not need to cause any disruption among services participants receive.

DOL has identified specific responsibilities for itself, national grantees and state grantees to ensure a smooth transition. DOL will provide orientation to all national grantees to provide information on program administration and management. DOL will begin regular conference calls between federal and regional DOL staff and national grantees to quickly address any transition issues. DOL will also provide assistance through a national call center, and provide on-site technical assistance as needed.

Question. Your budget proposes to save \$44 million in the Community Service Employment for Older American program through “efficiencies related to program streamlining.” What exactly is being proposed to save this amount?

Answer. The Administration proposes that reauthorization of the Title V SCSEP program be based on five key reform principles: (1) helping meet employers’ demands for skilled workers by attracting more older workers into the labor force, encouraging others to remain in the workforce, and by offering opportunities for older workers to update their skills; (2) making the One-Stop Career Center system effective for older individuals seeking to work or upgrade their skills, including better integrating services for older workers and assisting more older workers, regardless of income, to gain skills that are in demand; (3) tailoring services to meet the needs of individual older workers by providing a range of training experiences, including community service employment, on-the-job training and classroom training, depending on the individual’s background and experience; (4) targeting SCSEP resources to those older workers most in need (primarily low-income older workers who lack the basic skills for private sector employment), while ensuring that others receive services through the One-Stop Career Center system; and (5) streamlining the program to make it easier to administer in order to improve program performance, serve more participants, and receive a return on investment for the federal taxpayers’ dollar.

In fiscal year 2007, savings from streamlining administration and other reforms will amount to an estimated \$44 million in the first year of implementation. Specifically, we expect that savings will be achieved from the following reforms:

- Revamping the SCSEP program structure so that states conduct a competition every three years to run the program in the state, which will simplify administration, eliminate duplication, and create a more comprehensive program.
- Eliminating fringe benefits for program participants (except accident insurance or benefits that may be required by law) to reinforce the training aspect of the program.
- Allowing SCSEP funding to be used for training (as opposed to wages) and allowing more flexible training options in addition to community service work experience.

In addition to savings from reforms through reauthorization, savings will also be realized through the current grant competition. The current Solicitation for Grant Applications encourages a regional service delivery architecture that will reduce redundancy and fragmentation of service delivery areas by requiring that applicants apply to serve an entire county instead of a portion, and generally requiring that applicants apply to serve contiguous counties if multiple counties are served.

It is important to note that the fiscal year 2007 request will continue to support 92,300 low-income elderly individuals, the same level as fiscal year 2006.

ADMINISTRATION AND MANAGEMENT

Question. Provide appropriations and full time equivalent staff for each of fiscal years 2003 through 2005 enacted, fiscal 2006 comparable, and fiscal 2007 budget request, for each of the components of the Administration and Management activity within the Departmental Management account, including: Department Budget Center; Center for Program Planning and Results; Human Resources Center; Information Technology Center; Civil Rights Center; Office of Security and Emergency Management and Business Operation Center. Provide the source, by Department of Labor agency and activity, of the FTE and funding for Working Capital Fund Programs, comparing fiscal year 2006 comparable with the fiscal year 2007 request.

Answer. The information for Administration and Management follows:

ADMINISTRATION AND MANAGEMENT BUDGET ACTIVITY DEPARTMENTAL MANAGEMENT SALARIES AND EXPENSES

[Amount in thousands]

Agency	Fiscal year 2003 enacted		Fiscal year 2004 enacted		Fiscal year 2005 enacted		Fiscal year 2006 comparable		Fiscal year 2007 request	
	AMT	FTE	AMT	FTE	AMT	FTE	AMT	FTE	AMT	FTE
Center for Program Planning and Results	\$6,352	4	\$6,076	9	\$5,537	8	\$5,438	8	\$5,562	8
Human Resources Center	3,650	23	3,473	23	3,502	24	3,445	24	3,573	24
Information Technology Center	12,414	60	12,954	56	11,624	50	9,346	37	9,755	37
Business Operation Center	2,652	16	2,026	14	1,959	11	1,778	11	1,825	11
Office of Security and Emergency Mgmt. ¹	6,944	6,875	1,893
Department Budget Center ²	1,776	15	2,362	19	2,056	18	2,116	18
Library	714	2	719	2	754	1	754	1	782	1
Federal Executive Board	170	2	173	2	176	2	206	2	210	2
Assistant Secretary for Administration and Management	4,239	5	5,956	5	6,500	10	7,590	10	7,923	10
Civil Rights Center ³	5,930	48	6,144	48	6,237	46	6,451	46	6,735	46

¹ Represents funding for Frances Perkins Building security enhancements. The fiscal year 2007 Request includes a comparative transfer of \$5 million from this budget activity to the Working Capital Fund for upgrading security and continuity of operations capabilities for the Department.

² Department Budget Center was transferred to Administration and Management budget activity from the Chief Financial Officer budget activity in fiscal year 2004.

³ CRC is funded from the Civil Rights Activity, rather than the Administration and Management Activity.

The information for Working Capital Fund follows:

DOL AGENCY WORKING CAPITAL FUND ASSESSMENTS

[In thousands of dollars]

	Fiscal year	
	2006 estimate	2007 request
ETA	14,987	17,942
ETA/TES	9,326	9,922
ESA	37,620	44,021
OSHA	22,851	25,235
EBSA	10,054	11,463
BLS	16,009	19,353
OIG	4,097	4,685
OSEC	14,458	16,730
VETS	2,832	3,207
SOL	6,396	6,646
ILAB	1,984	2,228
MSHA	11,237	13,564
ODEP	1,250	1,305
FPB repairs	915	833
Total	154,016	177,134

PROGRAM DIRECTION

Question. Provide appropriations and full time equivalent staffing for each of fiscal years 2003 through 2005 enacted, fiscal 2006 comparable, and fiscal 2007 budget request, for each of the following components of the Program Direction and Support activity within the Departmental Management account: Office of the Secretary; Office of the Deputy Secretary; Office of Public Affairs; Office of the Assistant Secretary for Policy; Office of Congressional and Intergovernmental Affairs; Office of Small Business Programs; Office of Public Liaison; Office of the 21st Century Workforce; and the Center for Faith-Based and Community Initiatives.

Answer. The information for Program Direction follows:

PROGRAM DIRECTION AND SUPPORT

[Amount in thousands]

PDS components	Fiscal year 2003 enacted		Fiscal year 2004 enacted		Fiscal year 2005 enacted		Fiscal year 2006 ¹ comparable		Fiscal year 2007 request	
	AMT	FTE	AMT	FTE	AMT	FTE	AMT	FTE	AMT	FTE
Office of the Secretary	\$3,669	17	\$3,015	12	\$4,639	21	\$4,859	17	\$5,068	20
Office of the Deputy Secretary	1,173	8	1,270	8	1,260	9	1,234	8	1,293	9
Office of Small Business Programs	1,021	9	1,097	9	1,289	8	1,344	7	1,659	8
Office of Public Liaison	840	8	895	7	949	6	1,004	6	1,072	6
Office of Congressional and Intergovernmental Affairs	4,232	32	4,456	32	4,420	27	4,651	24	5,258	27
Office of Public Affairs	4,003	26	5,861	35	3,612	28	3,772	26	4,812	28
Office of the Assistant Secretary for Policy ²	10,423	53	8,975	46	8,903	40	7,222	35	8,741	40
Office of the 21st Century Workforce	1,019	8	1,049	8	1,041	6	1,040	6	1,092	6
Center for Faith-Based & Community Initiatives	593	5	605	6	633	6	800	6

¹ \$28.5 million was appropriated in ETA Program Administration for Job Corps program salaries and expenses. These funds have been allotted to the Office of the Secretary to be used for the Job Corps program in accordance with Section 102 of Public Law 109-149.

² Includes ASP drug-free workplace funds.

BUILT-IN AND PROGRAM CHANGES

Question. Provide a table for each discretionary appropriation account, identifying by line-item, the built-in changes from the fiscal year 2006 adjusted level, and each program increase, to arrive at the fiscal year 2007 budget request level.

Answer. The attached table reflects built-in increases and decreases, program increases and decreases, and finance changes, affecting each discretionary appropriation account from the fiscal year 2006 adjusted level to the fiscal year 2007 budget request level.

DEPARTMENT OF LABOR
[In thousands of dollars]

Discretionary Appropriation Account	Fiscal year 2006 adjusted level	Built-in		Program		Transfer	Finance changes	Fiscal year 2007 budget request—cur- rent Law
		Increases	Decreases	Increases	Decreases			
EMPLOYMENT & TRAINING ADMIN:								
TRAINING AND EMPLOYMENT SERVICES:								
Adult Employment and Training Activities	857,079				— 145,079			712,000
Dislocated Worker Employment and Training Activities	1,337,553				— 222,971			1,114,582
Youth Activities	940,500				— 100,000			840,500
Job Corps:								
Operations	1,450,400	1,282			— 50,080			1,401,602
Construction and Renovation	106,920				— 6,920			100,000
Subtotal—Job Corps	1,557,320	1,282			— 57,000			1,501,602
Responsible Reintegration for Young Offenders								
Prisoner Re-entry	49,104				— 49,104			
Native Americans	19,642							19,642
Migrants and Seasonal Farmworkers	53,696				— 2,238			51,458
Subtotal	79,252				— 79,252			
National Programs:								
Pilot, Demonstrations and Research	29,700				— 12,000			17,700
Evaluation	7,857				— 2,936			4,921
Denali Commission	6,875				— 6,875			
Other	1,980				— 1,980			
Community College Initiative				150,000				150,000
Subtotal—National Programs	46,412			150,000	— 23,791			172,621
Job Corps Construction Balances Cancellation								
Total—Training and Employment Services	4,940,558	1,282		150,000	— 754,435			4,337,405
COMMUNITY SERVICE EMPLOYMENT	432,311							432,311

DEPARTMENT OF LABOR—Continued
[In thousands of dollars]

Discretionary Appropriation Account	Fiscal year 2006 adjusted level	Built-in		Program		Transfer	Finance changes	Fiscal year 2007 budget request cur- rent Law
		Increases	Decreases	Increases	Decreases			
STATE UI & ES OPERATIONS:								
Unemployment Compensation (Trust Funds):								
State Operations	2,497,770							
AWIU	41,580	101,905		40,000				2,639,675
National Activities	9,900			600				10,500
Subtotal—Unemp Comp.	2,549,250	101,905	—41,580	40,600				2,650,175
Employment Service:								
Grants to States:								
Federal funds	22,883				—867			22,016
Trust Funds	693,000				—26,247			666,753
National Activities (Trust Funds)	33,428				—510			32,918
Subtotal—Employment Service	749,311				—27,624			721,687
One Stop Career Centers /ALMIS								
Work Incentives Grants	81,662				—17,807			63,855
	19,514				—19,514			
Total—State UI & ES Operations	3,399,737	101,905	—41,580	40,600	—64,945			3,435,717
Program Administration:								
Adult Services	43,360	1,716						44,788
Trust Funds	7,846							8,134
Youth Services	38,565	1,410						39,975
Workforce Security	6,225	2,616						6,426
Trust Funds	72,113			6,000				82,801
Apprenticeship Training, Employer and Labor Services	21,538	800						21,415
Executive Direction	6,956	320						6,156
Trust Funds	2,090							1,859

Total—Program Administration	198,693	6,862	6,000	—1	211,554
Total—ETA	8,971,299	110,049	—41,580	196,600	—819,380	—1	8,416,987
EMPLOYEE BENEFITS SECURITY ADMINISTRATION:							
Enforcement & Participant Assistance	111,604	3,794	—98	5,000	120,300
Policy & Compliance Assistance	17,358	642	18,000
Executive Leadership, Program Oversight & Administration	5,044	229	5,273
Total—EBSA	134,006	4,665	—98	5,000	143,573
EMPLOYMENT STANDARDS ADMIN.:							
Enforcement of Wage & Hour Standards	166,408	5,170	6,000	177,578
Office of Labor Management Standards	45,912	1,974	4,520	52,406
Federal Contractor EEO Standards	81,645	3,012	—1,000	83,657
Federal Programs for Workers' Comp.	99,593	4,581	104,174
Trust Funds	2,034	42	2,076
Program Direction & Support	17,253	550	400	—677	17,526
Total—ESA	412,845	15,329	10,920	—1,677	437,417
OCCUPATIONAL SAFETY & HEALTH:							
Safety & Health Standards	16,462	430	16,892
Federal Enforcement	173,430	6,503	179,933
State Programs	91,093	91,093
Technical Support	21,435	957	22,392
Compliance Assistance:							
Compliance Assistance—Federal	72,545	1,396	2,616	76,557
Compliance Assistance—State	53,357	53,357
Training grants	10,116	—10,116
Subtotal—Compliance Assistance	136,018	1,396	2,616	—10,116	129,914
Safety and Health Statistics	24,253	521	7,500	32,274
Executive Direction	10,591	578	11,169
Total—OSHA	473,282	10,385	10,116	—10,116	483,667
MINE SAFETY & HEALTH ADMIN:							
Coal	117,463	2,932	120,395

DEPARTMENT OF LABOR—Continued
[In thousands of dollars]

Discretionary Appropriation Account	Fiscal year 2006 adjusted level	Built-in		Program		Transfer	Finance changes	Fiscal year 2007 budget request cur- rent law
		Increases	Decreases	Increases	Decreases			
Metal/Nonmetal	68,227	1,879	70,106
Standards Development	2,485	173	2,658
Assessments	5,405	161	5,566
Educational Policy and Development	31,749	1,177	32,926
Technical Support	25,609	804	1,000	27,413
Program Eval & Info Resources	15,532	203	1	5,735
Program Administration	11,938	1,099	13,037
Total—MSHA	278,408	8,428	1,000	287,836
BUREAU OF LABOR STATISTICS:								
Employment & Unemployment Statistics	165,683	5,373	171,056
Labor Market Information (Trust Funds)	77,066	1,960	7,026
Prices and Cost of Living	173,515	5,566	8,000	187,081
Compensation and Working Conditions	81,052	2,808	83,860
Productivity and Technology	10,777	341	11,118
Executive Direction & Staff Services	30,235	912	31,147
Total—BLS	538,328	16,960	8,000	563,288
DEPARTMENTAL MANAGEMENT:								
Program Direction and Support	25,759	1,320	— 152	2,868	29,795
Departmental IT Cross Cut	29,462	— 57	29,405
Departmental Management Cross Cut	1,683	— 575	1,108
Legal Services	80,416	3,246	1,204	84,866
Trust Funds	308	14	322
International Labor Affairs	72,567	651	— 26	— 60,829	12,363
Administration & Management	30,613	1,237	— 4	— 100	31,746
FPB Security Enhancements	1,875	18	1,893
Adjudication	27,243	1,700	— 12	28,931
Women's Bureau	9,763	456	— 71	— 800	9,348
Civil Rights Activities	6,451	284	6,735

Chief Financial Officer	5,340	239	5,579
Total—DM S&E	291,480	9,165	—265	4,072	—62,361	242,091
OFFICE OF DISABILITY EMPLOYMENT POLICY	27,695	558	—7,934	20,319
VETERANS EMPLOYMENT AND TRAINING:										
State Administration Grants	160,791	427	161,218
Federal Administration	30,211	2,206	32,417
Nat'l Veterans Training Institute (NVTI)	1,964	5	1,969
Homeless Veterans Program	21,780	58	21,838
Veterans Workforce Investment Program	7,425	20	7,445
Total—VETS	222,171	2,716	224,887
OFFICE OF INSPECTOR GENERAL:										
Program Activities	65,744	2,329	68,073
Trust Funds	5,552	136	5,688
Total—OIG	71,296	2,465	73,761
Working Capital Fund	6,168	16	13,954
Total—DM	618,810	14,920	—265	10,092	—68,545	575,012
Total—Department of Labor	11,426,978	180,736	—41,943	241,728	—899,718	—1	10,907,780

WOMEN IN APPRENTICESHIP

Question. The conference agreement on the fiscal year 2006 Labor Department appropriations legislation specified \$982,000 for carrying out Public Law 102-530, the Women in Apprenticeship and Non-Traditional Occupations Act.

What action is being taken to issue grants to community based organizations to encourage employment of women in apprenticeable occupations and nontraditional occupations?

Answer. The Employment and Training Administration and the Women's Bureau have worked collaboratively to develop a Solicitation for Grant Applications (SGA). The SGA is currently going through Departmental clearance and we expect a notice announcing the SGA to be published in the Federal Register in August 2006.

APPALACHIAN COUNCIL/WORKING FOR AMERICA INSTITUTE

Question. This subcommittee held a hearing on July 22, 2004, on the funding of the Appalachian Council and Working for America Institute. Despite that hearing, the Labor Department did not renew the contracts for these organizations, forcing Congress to earmark \$2.2 million and \$1.5 million, respectively, for their continued operation. I understand that funding has now run out, and I urge you to renew the contracts. Will you take another look at the organizations, and see what can be done to provide renewed funding?

Answer. On February 1, 2005, the Department of Labor executed a \$1,500,000 grant to the Working for America Institute (WAI). This grant will remain active until February 3, 2007. The Department of Labor continues to work closely with WAI to support the deliverables of their grant, including developing resources to support a well-skilled advanced manufacturing workforce.

Job Corps funded the Appalachian Council for \$2.2 million in February, 2005 and then renewed the funding in the amount of \$2.2 million in April, 2006. That funding is through March 31, 2007. An evaluation will be done to determine if additional funding will be provided based upon performance and funding availability.

JOB TRAINING STAFF

Question. Your budget request for federal administration of Employment and Training Administration programs provided for 1,158 direct full-time equivalent staff, compared to the current level of 1,194 staff.

Why are you requesting only a reduction of 14 federal staff when you are proposing to consolidate several job training programs into a single block grant to states?

Answer. The Employment and Training Administration (ETA) fiscal year 2006 FTE level supported by appropriated funds is 1,180 (with an additional 16 FTE supported by fees and reimbursements). The ETA fiscal year 2007 Legislative Proposal FTE level (excluding FTE supported by fees and reimbursements) is 1,158. Compared with fiscal year 2006 staffing, ETA's fiscal year 2007 Legislative Proposal represents a net reduction of 22 FTE—an addition of 7 FTE within Youth Services to support the proposed transfer of Youthbuild from the Department of Housing and Urban Development to ETA, and a reduction of 29 FTE in Workforce Security in anticipation of the enactment of a Foreign Labor Certification Permanent Program fee.

ETA does not anticipate that the implementation of the Career Advancement Accounts (CAA) will have an immediate impact on ETA staffing levels. Assuming the passage of authorizing legislation in fiscal year 2007, a significant amount of effort by ETA staff will be required to transition from the current Workforce Investment Act (WIA) structure to a new CAA structure. Moreover, during the transition and until it is complete, the same or a similar level of effort that is currently provided will be necessary to continue national and regional Federal oversight required to administer WIA. The time necessary to implement the transition to a new CAA structure will also provide ample time for an orderly transition to an FTE level appropriate for the level of Federal oversight required to administer CAAs.

SAFE PLACES IN MINES

Question. The Commonwealth of Pennsylvania has begun an analysis of locating safe places in the mines for workers to seek refuge in case escape routes are blocked. These safe places could be permanent or portable. Do you intend to conduct a similar analysis nationwide?

Answer. Section 13 of the MINER Act requires NIOSH to study various refuge alternatives in an underground coal mine environment and issue a report not later than 18 months after enactment of the Act. Not later than 180 days after the receipt

of this report, the Secretary of Labor is required to provide a response to the two authorizing committees describing what actions, if any, the Secretary intends to take based on the report. The Department will comply with this statutory requirement.

COMPETITIVENESS AGENDA

Question. You propose cutting \$653 million from workforce investment programs and another \$27 million from the Employment Service, despite the fact that funding for workforce programs is \$1 billion below the funding level than when the President took over and there are one million more unemployed workers than there were in 2001. Isn't that approach inconsistent with a competitiveness agenda that is supposedly going to help America, and its workers, compete in the global economy?

Answer. Although the President's fiscal year 2007 Budget request for the Employment and Training Administration is below the fiscal year 2006 appropriation, it is a responsible budget that reflects the competitive demands for very limited resources for domestic programs and the need to eliminate waste and redundancy. The proposed reforms align with the competitiveness agenda by reforming the workforce investment system so that many more workers are trained, equipping them with the skills necessary to succeed in the 21st Century.

The public workforce investment system could be structured to better meet the training challenges presented by the increased need for skills and competencies by workers. There exists a lack of integration, which causes too much money to be spent on competing bureaucracies, overhead costs, and unnecessary infrastructure, and not enough on meaningful skills training that leads to job growth and economic prosperity.

Career Advancement Accounts, relative to the existing workforce investment system, will be more effective and flexible in meeting the demands of the global economy and in addressing the nation's workforce challenges. Career Advancement Accounts would mean a streamlined workforce investment system that gets more training dollars in the hands of workers and reduces costs by eliminating duplication across employment and training programs and lowering overhead costs. The greater efficiency from this redesign of the system will result in cost savings that account for much of the reduction in ETA's budget. More than triple the number of workers currently being trained would be trained under this proposal.

VOUCHER PROPOSAL

Question. You have proposed a new WIA reauthorization proposal calling for Career Advancement Accounts, i.e. vouchers, to be run through a consolidated workforce system overseen by the Governor, allowing him or her to choose to eliminate the local workforce system and the One Stop network. This is the third different reauthorization proposal you have made to the Congress, your previously two attempts to create a block grant for the Governor have been resoundingly rejected in both the House and Senate, which have consistently protected the local workforce delivery system as essential to helping our workers receiving training for jobs in the local economy. Knowing that this approach has been rejected twice before, isn't your budget proposal just a smokescreen to provide a rationale for deep budget cuts to the workforce system?

Answer. No. Under the Administration's proposal for Career Advancement Accounts, states can maintain One-Stop Career Centers to provide employment services to job seekers and employers, as well as access to Career Advancement Accounts, at these sites. Career Advancement Accounts are a more efficient and effective way to deliver job training that will result in more workers getting the skills they need with less overhead costs. We believe that with the constraints on discretionary spending and the promise of more than tripling the number of workers trained with this innovative new approach, Congress will take this proposal seriously. This proposal is consistent with the "innovation" agenda that has bi-partisan support in Congress.

Workforce Investment Act (WIA) reauthorization has been pending in Congress for three years. No proposals have been either formally accepted or rejected. H.R. 27, which was passed by the House on March 2, 2005, does consolidate the WIA Adult, WIA Dislocated Worker, and Employment Service funding streams, indicating interest on the part of Congress in streamlining programs as the Administration proposed.

RATIONAL FOR WORKFORCE TRAINING

Question. You claim that only 200,000 are trained annually by the workforce system; however your data provides the smallest data pool possible to make your claim,

as it only measures participants leaving training during a fiscal year. GAO estimates that over double this number, 416,000 receive training annually. Your own data provided in the Budget Justifications shows that over 15 million participants receive an array of training, intensive, or basic employment assistance annually through the workforce system. Isn't your budget request another example of using selective data to block grant and cut program funding?

Answer. The important point is that 200,000 people complete and exit training per year with a \$4 billion investment, meaning that too much money is being spent on low-cost services with little value to the customer. ETA uses actual data collected from the states in referencing number of people trained. The GAO study indicates that 40 percent of funds are used for training adults and dislocated workers, whereas ETA estimates this figure at 26 percent. This discrepancy occurs due to two primary differences in the measurements: (1) ETA is measuring exiters, or those that have actually completed training, while GAO is measuring training costs of all participants receiving training (meaning that people are "double counted" because their training may have occurred over two program years); and (2) ETA includes expenditures, while GAO includes both expenditures and obligations—obligations which may not result in someone actually being trained. The estimates by ETA and GAO are different because they look at distinctly different sets of cost estimates and individuals included in the count.

The question also refers to the number of individuals served by the workforce investment system. The large majority of these participants are receiving only basic employment services, including self-services. The Career Advancement Accounts proposal would increase the number of individuals trained through the workforce investment system, while still providing basic employment services to job seekers.

ELIMINATION OF MIGRANT PROGRAMS

Question. For the third year in a row, you have proposed eliminating the Migrant and Seasonal Farmworker program authorized under WIA. You first proposed to work with states and local areas to ensure that migrant and seasonal farmworkers could access services through One-Stop Career Centers; despite the fact that your Department's data show that the program met its performance goals. Now you propose to give governors the flexibility to design how individuals will access information and Career Advancement Accounts or vouchers. How does the Administration propose to ensure that these individuals—some of America's neediest adults and their families—will be able to successfully navigate among service delivery systems that will differ from state to state and secure the job training and employment services that they need?

Answer. The Administration's fiscal year 2007 Budget proposal seeks to tap the workforce investment system's potential to serve more migrant and seasonal farmworkers by providing job training services to them through the One-Stop Career Center system, and turning to other, appropriate agencies to provide supportive services, housing, and other related assistance. Currently, the section 167 program provides employment and training services to only 10,000 of an estimated 2 million farmworkers, which demonstrates the need for a wider system approach.

The Administration believes that providing services to farmworkers through the One-Stop system will increase the number served and have a positive employment and earnings impact on those who receive services.

The Administration's fiscal year 2007 budget proposal seeks to take advantage of the One-Stop system's potential to better serve more migrant and seasonal farmworkers by helping them access the full array of employment and training services available from the seventeen federal programs delivered through the One-Stop system. While the proposal is to increase the amount of funding spent on training utilizing Career Advancement Accounts as the vehicle, the proposal also includes continued funding for core service delivery, including career guidance and job referrals, to any job seeker. Career Advancement Accounts can be used for a combination of remedial training leading to a diploma or GED in addition to post secondary education. We believe this combination of career guidance and training in the context of the One-Stop delivery system that connects workers to a wide array of services, including supportive services, can result in increased services to farmworkers and more positive employment and earnings impact on those farmworkers who receive services.

EMPLOYMENT SERVICE CUTS

Question. You propose to cut the Employment Service by about \$27 million in fiscal year 2007 over and above a \$96 million reduction in fiscal year 2006. You would give states the flexibility to determine how to provide basic employment services to

America's workers and at the same time, absorb other costs that you propose to divest from the federal level—in labor market information products and services and dedicated professionals to help the disabled obtain employment. Past shortfalls in federal support have forced states to close local offices. With these deep cuts, states will be forced to shut down many more One Stop Career Centers that help match job seekers and employers seeking workers. How do you expect governors to be able to help an expected 14 million workers who need jobs and the thousands of employers looking for workers?

Answer. The Department proposes to consolidate the Workforce Investment Act (WIA) programs for adults, dislocated workers, and youth, and the Wagner-Peyser funding stream into a single flexible grant that enables governors to utilize these resources strategically to both drive their economies and provide maximum training and employment opportunities for their citizens.

The public workforce investment system, as currently constituted, is ill-equipped to meet the workforce challenges presented by the increased need for advanced skills and competencies in the 21st century economy. As one researcher has noted, "As it now stands, employment services (and by extension the One-Stop system) is very far from being an effective labor exchange capable of assisting people surmount the challenges of today's job market."¹ This is due, in part, to the lack of integration, which causes too much money to be spent on competing bureaucracies, overhead costs, and unnecessary infrastructure, and not enough on meaningful skills training that leads to job growth and economic prosperity. For example, while the Employment Service is intended to be the cornerstone of the One-Stop system under WIA, many states continue to have a separate network of Employment Service offices that offer the same "core services" that are available under WIA through One-Stop Career Centers.

Furthermore, large amounts of state unexpended carryover funds still remain. In fiscal year 2004, unexpended funds from the WIA Adult, Dislocated Worker, and Youth programs totaled almost \$1.2 billion and a similar amount is projected for fiscal year 2005, which ends on June 30, 2006. Therefore, it is the Administration's position that through more efficient administration, integration of existing funding, and the effective use of currently available resources, states will not face the need to reduce services to the citizens generally or to populations with barriers to employment.

NATIONAL RESERVE FUND

Question. Your proposal indicates that the Department would retain at the national level a portion of funds for a National Reserve Fund for unexpected emergencies before allocating funds for Career Advancement Accounts. What is the Department's estimate for this fund? And how would we distinguish the uses of these funds from the pilot, demonstration, and research account?

Answer. Under the Career Advancement Account (CAA) proposal, the Department proposes to set aside funds for a National Reserve in a manner similar to the current Dislocated Worker National Reserve structure. The Department would reserve 7.5 percent of the appropriation provided by Congress for Career Advancement Accounts for the National Reserve. The Secretary would have the discretion to use this funding to quickly address unanticipated events, such as natural disasters, mass layoffs and plant closings, and the impacts of foreign trade. The National Reserve would also be used to provide technical assistance and for demonstration activities.

The proposed use of Career Advancement Account National Reserve funds for demonstrations in addition to those carried out under pilots, demonstration and research budget authority is no different than the current structure. Under WIA section 171(d), up to ten percent of the National Reserve is used for dislocated worker projects. These demonstrations are in addition to the pilots, demonstrations and research authorized under WIA section 171(b). As it does now, the Department will maintain rigorous financial controls that track fund sources for all programs and activities.

RAPID RESPONSE SERVICES

Question. Your consolidation proposal eliminates state resources set aside specifically for states to respond rapidly with information and services to workers who have received word of pending layoffs. You would require states to apply for funds from the National Reserve Account to provide such services. What justification do you provide states about requiring them to go through extra steps to provide rapid

¹ Osterman, Paul. "Employment and Training Policies: New Directions for Less Skilled Adults." Paper prepared for the Urban Institute. October 2005. p.16.

response services and gaining their confidence that the Department can respond to such requests in a timely manner?

Answer. The Department does not contemplate that a state would have to apply for funds each time there is a mass layoff or to only sporadically fund a state rapid response coordinator. Early intervention to provide information and assistance to workers to decrease the amount of time between actual layoff and re-employment is a key principle of the dislocated worker program. Rapid response is a key element of this early intervention strategy.

States could demonstrate need and apply for rapid response funds at the beginning of the program year or throughout the program year. We will not propose that a state be required to submit an application for funding each time a dislocation event occurs.

In spite of all the good work that has been done over the past fifteen years with dislocated worker rapid response funds, the Department has found that most company executives do not know about the type and quality of assistance available to them and their employees when closures or layoffs are contemplated. They have also reported that where they have layoffs in several states simultaneously, the levels and quality of assistance varies dramatically. ETA, in collaboration with state and local partners, has undertaken several initiatives in the auto, textile and defense industries recently to try to integrate services and develop more consistency. We believe a nationally-coordinated approach to delivering rapid response assistance by states can help bring the services to more workers and employers.

The proposed mechanism will assist both the Department and the states to better manage scarce taxpayer resources by directing the bulk of the funds to the areas of need. For example, not all states experience major layoffs every year. Analyses of dislocated worker program expenditures reported by states have shown that the funds reserved for rapid response are consistently under-expended. In the aggregate, the rapid response carry-in funds from program year 2003 to 2004, and from 2004 to 2005, was \$136.7 million and \$166 million, respectively. Through March 31, 2006, states reported accrued expenditures of just over \$176 million of a total available of more than \$342.5 million, or 51.4 percent of the total funds available. States are not required to retain the up to 25 percent authorized to be reserved for rapid response activities. They may include a portion of the funds in the amount allocated to local workforce investment boards for core, intensive and training services for dislocated workers, or they may award additional funds from the reserved amount to local areas that experience disasters, mass layoffs, plant closings or other events that precipitate substantial increases (defined by the state) in the number of unemployed workers.

ADULT TRAINING FUNDS

Question. We need to upgrade the skills of our current workforce, including the low skilled on a broad base to increase economic growth and incomes. Recent data released from the National Assessment of Adult Literacy indicates that 14 percent of American adults had less than basic literacy skills—meaning they had a hard time locating easily identifiable information on commonplace material or following written instructions in simple documents. Your proposal would reduce adult training funds and turn the funds that are left into Career Advancement Accounts. It appears that low skilled adults who would compete with other workers for these vouchers may require combinations of assessment, career planning and developmental education services prior to being able to benefit from technical training. How will these individuals really fare under a system of capped vouchers and high pressure sales from many training providers?

Answer. We agree there is a need to upgrade the skills of our current workforce, including those with low skills and literacy. State and local workforce systems set service priorities, and this will continue to be the case under the CAA proposal. These priorities will differ across the country, since demographics, labor markets and regional economies differ. By combining funding streams, our proposal will allow a more flexible response to these differences. Our proposal will triple the number of workers who currently are being trained by the workforce investment system.

Assessment, career planning and developmental education services will continue to be accessed through One-Stop Career Centers, provided either through Workforce Investment Act funding or One-Stop partner programs. States will be responsible for determining eligible training providers within the state, as well as determining policies that govern those providers, such as policies to prevent false advertising and other abuses.

ECONOMIC GROWTH EFFORTS

Question. Your consolidation proposal, combined with sizable cuts and program eliminations, ironically puts states in the position of not being able to jump start or continue to nurture regional economic growth planning and collaboration activities that integrates economic development, workforce development and education systems. These activities are similar to those you are promoting through your new WIRED initiative. What do you say to states that want to move forward with such integrated economic growth efforts if they don't qualify for funds under federal rules?

Answer. The proposals for consolidation of workforce programs are intended to provide maximum flexibility for states and regional economies to implement the type of workforce investment services that are needed in that specific region. We believe that our traditional thinking about how individual programs are funded is contributing to the persistent problem of siloed program services, with excessive funds being spent on overhead and bureaucracy, rather than addressing the workforce needs of a regional economy. If regional economic needs are to be effectively and comprehensively addressed, it will take many sources of funding, including funding from economic development agencies and educational institutions, and coordination across these funding streams. Therefore, the approach of making Federal funding for workforce services more flexible will contribute to integrated economic development efforts and the maximum leveraging of resources. Finally, the transformation of a regional economy is not dependent on Federal demonstration funding. What drives transformation is the collaborative leadership and strategic planning of economic development, research and development, capitalization, entrepreneurship and workforce development visionaries.

ELIMINATION OF YOUTH TRAINING GRANTS

Question. Your proposal to redesign the workforce delivery system eliminates WIA training grants for disadvantaged youth that are aimed at improving their education, employment, and earnings prospects. It is difficult to reconcile your proposed request when the President and you as well have focused on the need to raise the skills of young people in order to maintain our competitive edge in this new global economy. And from research—much funded by your Department, we know that an array of services is necessary to help disadvantaged youth complete their education, mature into solid citizens, and make the successful transition to work. By making these young people compete with adults for Career Advancement Accounts, aren't you really limiting their changes for future success?

Answer. We agree that there should be an emphasis on raising the skills of young people in order to maintain our competitive edge in the global economy. Career Advancement Accounts will be available to out-of-school youth. Furthermore, states and localities will still be able to provide career counseling and other services to these out-of-school youth, and workforce information will be available to assist them in choosing careers in high growth industries and in determining appropriate training for those careers.

Targeted programs and set-asides have led to multiple program silos, excessive overhead and bureaucracy, lack of coordination and integration, and only a modest number of people trained for the size of the workforce system investment. States and local areas will still be able to serve targeted groups, such as out-of-school youth, but will have more flexibility in using resources and not be subject to the often conflicting requirements of multiple programs or funding streams. Furthermore, consolidating funding streams will enable states and localities to better focus on the needs of their distinct populations, since labor force demographics and labor markets vary considerably across the country. The substantial number of requests for waivers to allow transfer of funds between programs indicates the need for more flexibility in this area than the current legislation allows.

CAREER ADVANCEMENT ACCOUNTS

Question. A recent ETR article on the fiscal year 2007 budget request noted "ETA officials said their legislative analysts believe this program—the consolidated Career Accounts proposal—can be implemented under current authorizing statutes, but would be easier for states to embrace with program consolidation that would occur under the WIA reauthorization package put forward by House Republicans, HR 27." It's my understanding that HR 27 has passed the House and is awaiting conference with the Senate. Please explain how, if the House already has a bill that is not consistent with your Career Advancement Accounts proposal, how you plan to accomplish this.

Answer. As you indicate, the House has passed H.R. 27 and the Senate recently passed its version of Workforce Investment Act reauthorization legislation. H.R. 27 would implement many key components of the President's job training reform proposal, such as merging funding streams. We believe CAAs can be built upon this piece of legislation.

ELIMINATION OF JOB BANK PROGRAM

Question. The elimination of America's Job Bank is particularly troubling. It is the backbone for more than 20 state job banks as well as the electronic version of a national employment service. Thousands of job seekers get their work through AJB and thousands of employers use it. By your own Department's last count, over 138 million job searches were conducted on AJB for the year ending June 3, 2005 and over 9 million resume searches were conducted by employers during the same period. There were about 7.8 million job postings originated on AJB during that year, over 700,000 new resumes posted, and 55,000 new employer registrations. All of these activity counts are increases over the prior year. How can the United States have a modern public employment service without an electronic exchange?

Answer. The Department of Labor considered numerous factors in coming to the decision to phase out America's Job Bank (AJB), which included looking at the larger environment in which AJB is operating and weighing the costs associated with running the system. Since the launch of AJB, the number of private sector Internet-based job banks (Career Builder, Monster, Yahoo! Hot Jobs, etc.) has proliferated, calling into question the need for a Federal government-sponsored national job bank. These private-sector electronic labor exchange systems are continuously improving and most, if not all, of these sites offer free services to job seekers. Current trends in the industry seem to indicate that some level of free service will also be offered to businesses/employers in the future and many employers who currently use AJB are already using these other job banks simultaneously to advertise their openings.

In addition, it has been increasingly difficult, if not impossible, to keep America's Job Bank updated as technology has advanced. Also, as Internet technology and technical resources have become widespread and the costs associated with them have declined, state and local areas that previously relied on AJB for their Internet self-service labor exchange presence have built and operate job banks of their own that are not based on AJB and promote them to their job seeker and business customers rather than AJB.

AJB is not the backbone for 20 state job banks, nor is there any evidence of widespread job gains as a result of using AJB. In fact, AJB is not used in most One-Stop Career Centers across the country.

PROPOSED WORKFORCE LEGISLATION

Question. The Administration plans to introduce legislation to reform the workforce investment system and create the Career Advancement Accounts (CAAs). If this legislation is not passed before fiscal year 2007, what would be the impact on services of the proposed 15 percent funding reduction for workforce development programs?

Answer. The President's Budget request assumes enactment of the Career Advancement Account (CAA) proposal, which would reduce overhead and administrative costs and focus more funding on training, thereby tripling the number of individuals receiving job training through the workforce investment system. In the absence of CAA legislation passed by Congress, the workforce investment system will continue to have siloed funding streams that result in duplicative costs.

While states will be able to continue operating Workforce Investment Act programs and the Employment Service at the lower funding levels proposed by the Administration, these reduced levels, without the accompanying reforms, may result in decreases in the number of participants served through these programs, compared to the President's proposal.

Question. States could administer the CAAs through "community career centers" at community colleges, public libraries, senior centers, and other locations, as well as through existing one-stop centers. Could this approach lead to the creation of a parallel system of job search and career assessment services, that duplicates what is already available through the one-stop centers? Could it lead to confusion among potential customers of the system, about where to go to access services?

Answer. Under our proposal, states can maintain One-Stop Career Centers to provide employment services to job seekers and employers, as well as access to Career Advancement Accounts. States and localities would have the option of making em-

ployment services and access to Career Advancement Accounts available at additional sites in the community.

Question. Will the existing state and local workforce boards have any role in administering the new program, or will they be disbanded? Similarly, will the programs that are currently mandatory partners in the one-stop system have any role in administering the CAAs?

Answer. State and local Workforce Investment Boards will continue to exist and retain roles and functions similar to what they have under the current Workforce Investment Act. Similarly, the required partners will continue to participate in the One-Stop service delivery system, and have a role in setting local policy and providing oversight for the service delivery system. The specific role of the partner programs in administering Career Advancement Accounts (CAA) would be worked out under policies set by the state in setting up the CAA system.

Question. How will the Labor Department calculate the amount of funds each state will receive for CAAs? Will there be a formula?

Answer. There will be a formula for allotting Career Advancement Account funds to states, similar to the formulas that have been used to allot funds to states under current law. The specific formula proposal has not been finalized, but the final formula would be worked out between the Administration and Congress.

Question. The CAA proposal assumes that individuals need minimal assessment and case management services to make good decisions about whether and how to use training funds. However, in implementing reform of the Trade Adjustment Assistance (TAA) program, you have emphasized the need to co-enroll TAA participants in WIA for case management, so that their training needs can be properly assessed. What is the basis for your decision to provide training funds with minimal case management funds, in the CAA proposal?

Answer. The Department's ongoing evaluation of the Individual Training Account activity under the Workforce Investment Act shows that when an individual is provided more choice in training and counseling services, the individual is more likely to use an ITA for training and to enter training more quickly. Further, the individual's training selection tends to be similar to training programs selected by similar individuals who are required to receive counseling services and approval.

We believe that up-front assessment (as contrasted with ongoing and costly case management) is what workers need, including those served under the TAA program. Assessments can be provided under the CAA proposal if needed, with over \$700 million set aside for such services to complement training (22 percent of the total consolidated resources per state, roughly equivalent to the current Wagner-Peyser amount for core services). The purpose of such assessments is to properly gauge marketable skills and assist workers to reenter employment or identify training to fill gaps in marketable skills. Our demonstrations show that with this "informed choice" more people can receive actual training for jobs in the local labor market.

Question. The new system would be designed based on lessons from the implementation of the Individual Training Account and Personal Reemployment Account (PRA) programs. What lessons specifically have been drawn from the implementation of those programs? What evaluations exist to support giving more control over training funds to individuals?

Answer. CAAs provide individuals with increased customer choice and flexibility for selecting training and other services that are appropriate for them and are based in part on lessons learned from Individual Training Account (ITA) and Personal Reemployment Account (PRA) demonstrations.

The ongoing evaluation of the ITA Experiment explored the use of increasing customer choice in the delivery of ITAs. Initial analysis from eight local boards participating in the experiment showed that when an individual was provided more customer choice in training and counseling services, the individual was more likely to accept an ITA for training, the individual's training selection tended to be similar to training programs selected by individuals required to receive counseling services and approval of programs, and the individual was more likely to enter training quickly. The final report, to be completed later this year, will provide a more in-depth analysis of the impacts of the three different ITA service approaches.

The goals of PRAs are to provide individuals who are identified as most likely to exhaust Unemployment Compensation with a quicker return to work, direct access to training, greater customer choice and control, and better economic outcomes. Initial observations from the PRA Demonstration show that participating states were able to implement the PRAs generally as planned, with the first accounts offered in March 2005. The evaluation of the PRA Demonstration is underway. An interim report, to be completed this year, will provide a more in-depth understanding of the implementation process. In the meantime, reports from states on best practices

show that account mechanisms can be implemented, appropriate oversight can be maintained, and individual choice can provide greater access to needed services.

Question. The CAA proposal includes performance measures that are similar to those now used to assess the adult and dislocated worker programs. However, with CAA funds going directly to individuals, who would be held accountable for performance outcomes—states or the local community career centers? Does it make sense to apply performance measures designed for adults (that focus on employment outcomes) to CAAs that are also used by youth? Currently, youth performance measures also consider educational goals.

Answer. States will continue to negotiate performance targets and report to the Department of Labor on three primary outcome measures: (1) entered employment, (2) retention in employment, and (3) earnings. In addition, attainment of a degree or certificate, entry into training and education, and literacy and numeracy gains would be tracked as intermediate outcomes.

RAPID RESPONSE FUNDS

Question. Currently, states use rapid response funds to provide immediate service to workers affected by a mass layoff, often before the workers are even laid off. Under your legislative proposal, states will need to apply to The Employment and Training Administration for rapid response funds as events occur. What are the reasons for keeping these funds at the national level, and having states apply for them each time they are faced with a mass layoff? What effect will this approach have on states' ability to provide immediate rapid response services for mass layoffs?

Answer. The Department does not contemplate that a state would have to apply for funds each time there is a mass layoff or to only sporadically fund a state rapid response coordinator. Early intervention to provide information and assistance to workers to decrease the amount of time between actual layoff and re-employment is a key principle of the dislocated worker program. Rapid response is a key element of this early intervention strategy.

States could demonstrate need and apply for rapid response funds at the beginning of the program year or through the program year. We will not propose that a state be required to submit an application for funding each time a dislocation event occurs.

In spite of all the good work that has been done over the past fifteen years with dislocated worker rapid response funds, the Department has found that most company executives do not know about the type and quality of assistance available to them and their employees when closures or layoffs are contemplated. They have also reported that where they have layoffs in several states simultaneously, the levels and quality of assistance varies dramatically. ETA, in collaboration with state and local partners, has undertaken several initiatives in the auto, textile and defense industries recently to try to integrate services and develop more consistency. We believe a national approach to delivering rapid response assistance by states can help bring the services to more workers and employers.

The proposed mechanism will assist both the Department and the states to better manage scarce taxpayer resources by directing the bulk of the funds to the areas of need. For example, not all states experience major layoffs every year. Analyses of dislocated worker program expenditures reported by states have shown that the funds reserved for rapid response are consistently under-expended. In the aggregate, the rapid response carry-in funds from program year 2003 to 2004, and from 2004 to 2005, was \$136.7 million and \$166 million, respectively. Through March 31, 2006, states reported accrued expenditures of just over \$176 million of a total available of more than \$342.5 million, or 51.4 percent of the total funds available. States are not required to retain the up to 25 percent authorized to be reserved for rapid response activities. They may include a portion of the funds in the amount allocated to local workforce investment boards for core, intensive and training services for dislocated workers, or they may award additional funds from the reserved amount to local areas that experience disasters, mass layoffs, plant closings or other events that precipitate substantial increases (defined by the state) in the number of unemployed workers.

FOREIGN LABOR CERTIFICATION

Question. There is an inherent unfairness to having some employers' applications from six years ago pending at the BEC and having new applications adjudicated in two months. These inordinate delays have caused and are causing serious prejudice to employers and employees alike. With this as background, please address the following issues:

Answer. The Department published a final regulation implementing a new re-engineered Permanent Labor Certification Program effective March 28, 2005. This regulation created a new faster and more efficient method for employers to have their applications processed. The regulation applies to all applications filed after its effective date. However, for applications previously filed up until March 27, 2005, those applications must be processed under the previous regulation. The process prescribed by the previous regulation takes considerably more time than the new one, despite efficiency measures we have introduced, e.g., technology, to streamline it as much as possible.

Question. Congress has expressed a clear intention in the Child Status Protection Act to prevent government delays from separating families by having children turn 21 during the permanent residence processing. At the time Congress passed the CSPA, the existing scope of the DOL backlog was unanticipated. In light of the clear Congressional intention, why has the Department of Labor refused to expedite long-pending backlogged applications based upon a showing that the impact of the delay will forever prevent a child from becoming a permanent resident with his or her parents?

Answer. We understand the Child Status Protection Act applies only to cases pending before the Department of Homeland Security. The Department of Labor strongly supports efforts to keep families together. The Department has determined this goal can best be accomplished by minimizing the amount of time it takes to process foreign labor certification applications. For this reason, the Department has consistently applied a first in/first out (FIFO) policy to cases in the Program Electronic Review Management (PERM) program. The FIFO policy prevents the need to make subjective decisions regarding which, if any, cases merit special consideration for expedition, thereby conserving resources and substantially reducing the amount of time that is required to process applications. It is ETA's longstanding policy to also process cases in the permanent labor certification program backlog on a "First-In/First-Out" basis within that system's various processing categories; for example Reduction in Recruitment (RIR) cases are in a separate processing queue from cases being handled through the traditional recruitment process (TR), but cases in each queue are processed on a "First-In/First-Out" basis. It has been ETA's established policy never to expedite cases based on the specific circumstances of individual employers or aliens.

Question. In addition to children aging out, other significant detriments to employers and employees exist in specific cases. Examples include inability to promote employees, loss of tuition benefits, inability to travel, inability for spouses to work, etc. Given that the delays are through no fault of the employer or the employee, why has the Department of Labor failed to establish a system for expediting worthy cases?

Answer. The Department's policy of not expediting cases saves an enormous amount of limited resources since we do not have to evaluate the merits of each request to expedite across what potentially could be tens of thousands of cases. Furthermore, we believe some of the concerns you note arise from visa restrictions over which the Departments of State and Homeland Security have jurisdiction and not from any DOL permanent labor certification rules or requirements.

The most equitable response to this complicated issue is to require strict adherence to our first-in/first-out policy under which all applicants are treated consistently. For every case considered for expedited consideration, an older case would be further delayed. Unlike the Department of Homeland Security, the Department of Labor does not have the legislative authority for a fee structure which allows for "premium processing."

Currently, employers do not pay a fee to DOL for the processing of permanent foreign labor certification applications. Employers benefit significantly from the admission of foreign workers, and the efficient review of applications they receive under the new, streamlined process. The backlog system is not fully automated and therefore continues to function through a FIFO process. The Administration has included a proposal in the fiscal year 2007 budget to create a fee structure for the Permanent Labor Certification Program. We anticipate revenue from such fees would permit the assignment of additional staff, such that there should be no backlogs in the new PERM system.

Question. Why has the Department of Labor made it so difficult and risky for employers to convert cases from the BEC to PERM? Seemingly, DOL has created the most restrictive rules possible to discourage these conversions, resulting in an unexpectedly low number of conversions and an unexpectedly high number of cases remaining at the BECs? Will DOL amend its rules to encourage conversions? Examples of improvements include eliminating the risk of the loss of priority date if a case is not eventually adjudicated to be "identical"; eliminating the risk of loss of

the ability to obtain seventh year H-1B extension if the case is not considered to be "identical"; removing the "identical" standard entirely; changing present procedures which involve audits of most or all of the conversion cases; eliminating the very extensive delays in adjudicating PERM conversion cases; and allowing cases at the BEC to remain pending until the approval of the PERM case (especially since a mere typographical error could result in a PERM case being denied).

Answer. The Department is in the process of reviewing the rate at which cases have been converting from the old pre-PERM certification system to PERM. Employers currently have the option of re-filing the case if it meets the requirements of the PERM regulation. Those who wish to have the benefit of the new efficient processing system must meet the regulatory requirements of that rule. The Department does not have the resources to process identical cases under two different regulations implementing the permanent labor certification program, i.e., pre-PERM and post-PERM. Removing the "identical" standard under the PERM regulation would require a new rulemaking process and has the potential for trading backlogs between the Backlog Elimination Centers and the Department's National Processing Centers. We do not feel that this would be in the interests of employers or foreign workers. The new PERM system is much more efficient than the old system, but converting all old cases into new PERM cases would result in backlogs in PERM.

Question. What is the plan for dealing with applications for which no 45 day letter was received by June 30? Will provisions be made for reconstructing lost files? When will employers be notified of these procedures?

Answer. The BECs have taken extensive steps to ensure that all applications identified for transfer to the BECs have been shipped and received at their designated destination. However, because there may be some applications that for various reasons were never identified by the state agencies or ETA Regional Offices for shipment to the BECs, we are developing a process by which to handle those cases. Within the past two weeks, the Department posted a detailed set of Frequently Asked Questions (FAQs) on the foreign labor certification website which addresses procedures related to the 45-day letters <http://www.ows.doleta.gov/foreign/#whatsnew>.

Due to the high demand for information and time and resource constraints, we believe that posting the information on our website is the best way for the entire public to have access to the information at the same time. These FAQs will provide procedures for employers in the event they have had a case closed through the non-receipt of a 45-day letter. Additional FAQs to cover these situations may be posted if appropriate at a later date.

Question. What are the realistic expectations for adjudicating all BEC cases by September 30, 2007? How are these expectations impacted by losses of the top level people at the BEC in Pennsylvania? How has DOL factored into these expectations the lack of incentive for BEC employees to complete the cases on a timely basis since doing so will result in loss of their positions as of September 30, 2007?

Answer. The Department has plans underway to fill all vacancies, both Federal and contractor staff, at the Philadelphia Backlog Elimination Center. Since establishing the two (2) backlog centers in July 2004, we have logged in all 360,000+ cases transferred to the backlog centers from the states, sent 45-day letters to all employers, and cleared over (157,473) cases from the centers. We intend to have all backlog cases under processing by September 30, 2007.